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INVESTIGATION OF THE CHARACTERISTICS OF THE PHILIPS TYPE OF MÜLLER METALIX TUBES AS REVEALED BY THE ROENTGENOGRAM[1]

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THE purpose of the investigation was to determine the class of work in which the Philips type of Müller Metalix tubes will produce better roentgenograms than the Coolidge tubes.

APPARATUS

For the investigation, two Müller Metalix tubes of the Philips type and five Coolidge tubes were used, as listed below, the focal spot sizes being measured by the pinhole method.

1. 3 K.W. Metalix Radiator, focal spot 3.5 x 3.5 mm.
2. 6 K.W. Metalix Water-cooled, focal spot 3.5 x 3.75 mm.
3. 10 milliamperes Coolidge, focal spot 3 x 3 mm.
4. 10 milliamperes Coolidge, focal spot 4 x 4 mm.
5. 30 milliamperes Coolidge, focal spot 4.75 x 5 mm.
6. 100 milliamperes Coolidge, focal spot 8 x 8.5 mm.
7. B. F. Universal, focal spot 7.5 x 11 mm.

The energy for the tubes was supplied by a double cross arm rectifying switch type of machine, with all exposure factors controlled and carefully checked.

[1]Read before the Philadelphia Roentgen Ray Society, March 7, 1929.

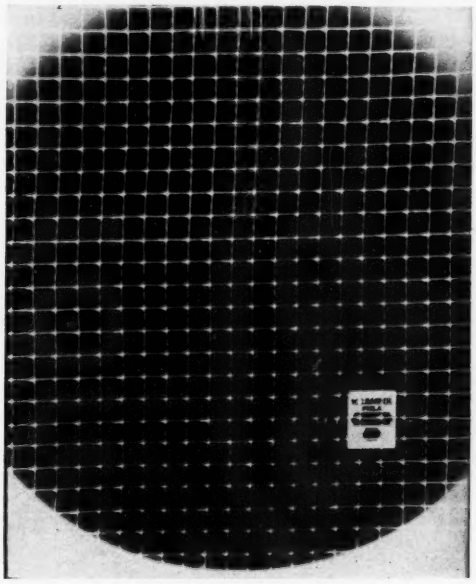

Fig. 1, Film No. 11. See text for description.

OBSERVATION OF DETAIL IN ROENTGENOGRAMS

To analyze the detail of structure, wire mesh was used. The distances that the mesh was raised from the films were chosen to represent the structures of the body usually examined. It was thought that the study of the wire mesh two inches away from the film would correspond to the ex-

TABLE I

WIRE MESH

Technic: 25 inches T.F.D., 47.5 K.V.P., 10 ma., 5 sec.; 35 inches T.F.D., 47.5 K.V.P., 10 ma., 10 sec.

	½ in. Mesh 25 in. T.F.D.			¼ in. Mesh 25 in. T.F.D.			½ in. Mesh 35 in. T.F.D.			¼ in. Mesh 35 in. T.F.D.			¼ in. Mesh 76 in. T.F.D.		¼ in. Mesh 64 in. T.F.D.	
	Object-film distance			Object-film distance			Object-film distance			Object-film distance				Obj.-film dist.		Obj.-film dist.
TUBE	2 in.	4 in.	6 in.	2 in.	4 in.	6 in.	2 in.	4 in.	6 in.	2 in.	4 in.	6 in.	TUBE	8 in.	TUBE	8 in.
W. C. 6 K.W. Line Focus	No. 3	No. 4	No. 5	No. 6	No. 7	No. 8	21	22	23	24	25	26	5/10 R.	62	5/10	51
Radiator 3 K.W. L.F.	9	10	11	12	13	14	15	16	17	18	19	20	5/100 R.	63	B.F.U.	52
5/10 Rad.	27	28	29	30	31	32	33	34	35	36	37	38	B.F. Univ.	64	Mesh Contact	
5/30 Rad.	39	40	41	42	43	44	45	46	47	48	49	50	F.F. Univ.	65	5/100 R. 3 K.W. L.	109 109

TABLE II

Skeleton—Pelvis								Skull	
	Philips tube 3 K.W. Rad.		6 K.W. W.C.						
	T.F. Dist.		T.F. Dist.			T.F. Dist.			
	25 in.	32 in.	25 in.	32 in.	TUBE	25 in.	32 in.	TUBE	T.F. Dist. 30 in.
Anode to Feet	88	100	92	96	5/10 R. 8/64	83	104	5/10 R. 8/64	135
Anode to Head	89	101	93	97	5/10 R. 10/64	84	105	5/10 R. 10/64	136
Anode to Left	90	102	94	98	5/30 R. 13/64	85	106	5/30 R. 13/64	137
Anode to Right	91	103	95	99	5/100 R. $\frac{20 \times 20}{64}$	86	107	5/100 R.	138
					B.F.U. $\frac{19 \times 28}{64}$	87	108	3 K.W. Rad.	139 A. to Feet.
								6 K.W. W.C.	140 A. to Feet.

Technic: 25 in. T.F.D., 10 ma., 30 sec., 47.5 K.V.P.
32 in. T.F.D., 10 ma., 21 sec., 55 K.V.P.

Technic: 10 ma., 80 K.V.P., 5 sec.

KEY: Figures after "Tube" refer to film numbers.

tremity group; six inches away from the film, to the pelvic structures; eight inches away from the film, to the structures in the chest, and to have an equivalent for various intermediate structures of the body, the wire mesh was examined four inches away from the film.

Wire mesh of half-inch squares seemed to be best for the study of the characteristics produced by the focal spot, but as the structures of the body are more compact, it was thought that a finer wire screen might improve the visibility, so a series of films was made of one-quarter inch square wire mesh. The diameter of the wire forming the screen of the half-inch mesh is approximately 1 mm. and that of the quarter-inch square mesh is approximately ½ mm.

Films (14 by 17 inches) were exposed over their entire surfaces, and to eliminate the possibility of poor contact, no screens were used.

Table I shows the set-up for the exposure of the wire mesh.

Figure 1 is a print of Film No. 11 made of the one-half inch square wire mesh, placed at a distance of 6 inches from the film, using a 3 K.W. Müller Metalix tube of the Philips type, at a target film distance of 25 inches. Because the diameter of the wire is less than the size of the focal spot, the source of light arises from a greater area than the size of the object, causing an umbra and penumbra effect. The rays given off from the heel of the anode arise from an area corresponding more nearly to that of the diameter of the wire, so that the shadows of the screens projected in this region do not show the umbra and penumbra effect. The tube was placed lengthwise, parallel with the long dimension of the films. It will, therefore, be noticed that at the lower part of the film, the one near the anode end of the tube, the cross lines of the shadows of the wire mesh are very sharply defined, while at the other end of the film, the shadows of the cross wires are somewhat blurred.

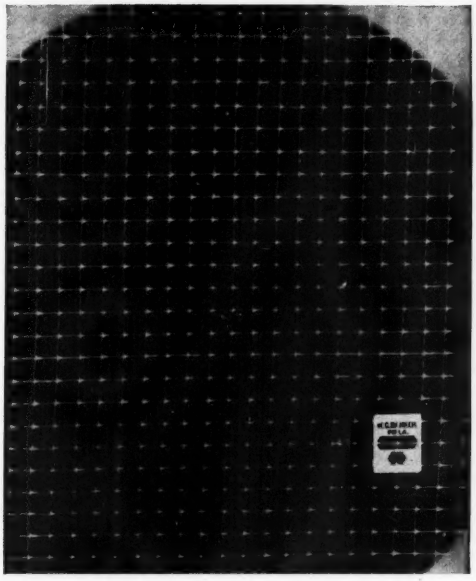

Fig. 2, Film No. 41. See text for description.

Figure 2, Film No. 41, made of the same wire mesh and under the same conditions, but using a 5-30 radiator type Coolidge tube, shows also the umbra and penumbra effect, but none of the individual cross wires are so sharply outlined as those projected from the heel of the Philips tube. There is some difference in the sharpness of the wire mesh at each end of the film, but it is not nearly so marked as in the film made of the wire mesh with the Philips tube.

These two roentgenograms demonstrate that the detail of the structure as projected from a Coolidge tube, at these distances, is more evenly distributed over a 14x17 in. film than it is when the Philips tube is used.

When the Philips tube was used at a target film distance of 35 inches, the uneven distribution of detail, while still present, was not nearly so noticeable, and when the Coolidge tube was used at this distance, the

Key: Figures after "Tube" refer to film numbers. Technic: 10 ma., 80 K.V.P., 5 sec.

shadows of the wire were much sharper and evenly distributed.

In the films made of the wire mesh only 2 inches away from the films, the variation in the distribution of detail over the film made with the Philips tube is much less noticeable, and the detail of the wire mesh made with the 5-30 radiator Coolidge tube approximates that of the Philips tube and is evenly distributed over the whole film.

This demonstrates that in the study of the structures within 2 inches of the films, the appearance of the detail is not much affected by the size of the focal spot, and that in the study of the structures removed 4 to 6 inches from the film, the detail is improved by increasing the target film distance.

The Philips tube is so constructed that the focal spot is greatly elongated, thereby distributing the heat over a greater area, and it is set at an angle of 19 degrees, so that the picture of the focal spot made by the pin-hole method is square, and when the size of the focal spot, as measured by this method, is equal to the size of a focal spot of a Coolidge tube made in the same manner, the Philips tube will carry more energy than the Coolidge tube.

Because the angle of the anode is 19 degrees and the focal spot elongated, it produces an effect on a 14x17 in. film as if the part of the film near the anode end of the tube were exposed by a very small focal spot tube, and the part of the film near the

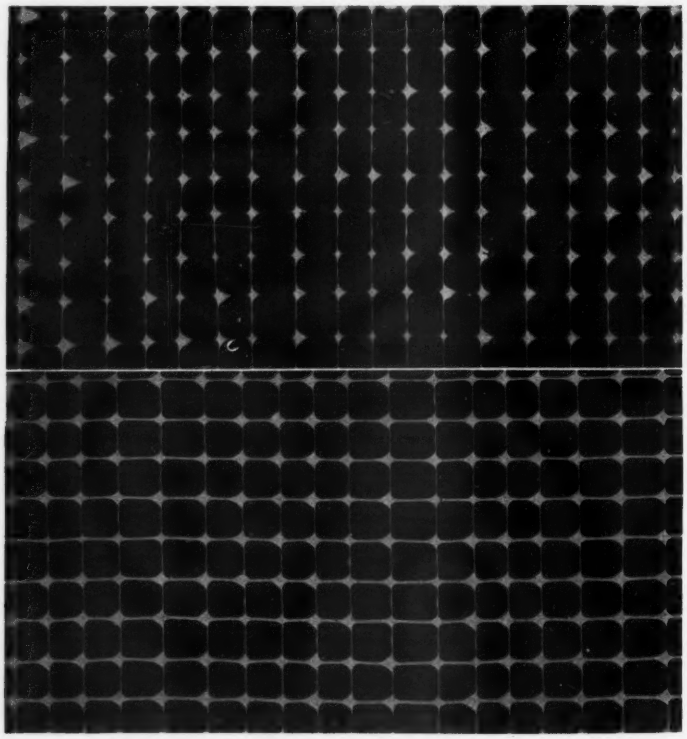

Fig. 3. Contact prints from 14 × 17 in. film, exposed to 3 K.W. Müller Metalix tube. *Lower print,* from section near anode end of tube: Horizontal lines broad and sharp, vertical lines not so sharply defined. *Upper print,* from part of film near the cathode end of tube: Horizontal lines blurred, vertical lines same as in lower print. This demonstrates the uneven distribution of detail.

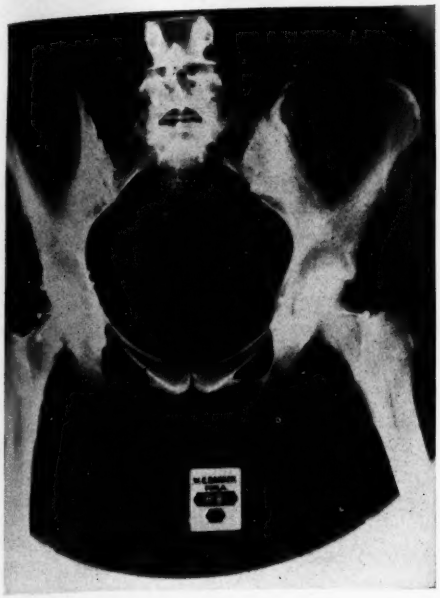

Fig. 4, Film No. 88. Dried specimen, made with 3 K.W. Metalix tube. Anode toward feet. See text for description.

Fig. 5, Film No. 89. Made of dried specimen with 3 K.W. Metalix tube. Anode toward the head. See text for description.

cathode end of the tube were exposed by a broad focus tube (Fig. 3). The shadows at the latter end of the tube are furthermore distorted because of the rectangular shape of the focal spot, which blurs the shadow more in one direction.

EXAMINATION OF LARGE AREAS OF THE BODY

The effect of this distortion is brought out when films are made of the dried bony pelvis.

In Figure 4, Film No. 88, with the anode of the 3 K.W. Philips tube toward the feet, the detail of the bony structure is good through the femurs and pubic portion of the pelvis, while at the crests of the ilia there is a loss of detail, particularly noticeable in one direction.

In Figure 5, Film No. 89, with the anode of the tube toward the head, the detail of the bony structure is good in the region of the spine and crests of the ilia, while through the femurs there is an uneven distribution of detail, it being sharper in one direction than in the other.

This variation in detail may be better observed in Figure 6, a contact print of the heads of the femurs made from the 14x17 in. film, exposed to the 3 K.W. Metalix tube with the anode toward the left. The detail is sharply defined in the left hip and blurred in the right hip. In Figures 7 and 8, Film No. 83, made with the 5-10 Coolidge tube, the detail is evenly distributed throughout the film.

The detail of the same pelvis examined at 32 inches target film distance with the Philips tube is more evenly distributed, but the variation is still quite noticeable.

In the films listed in Table III, made of the pelvis of the living subject, the uneven distribution in detail is still noticeable, but the secondary radiation added from the soft structures, blurring detail generally, makes

this disadvantage of the Philips tube less noticeable than in the dried specimen.

Undoubtedly, in the examination of areas covering a 14x17 in. film when the elongated rectangular focal spot tube is used, the films are not so good for diagnostic purposes as those made with the Coolidge.

TABLE III

PELVIS (LIVING SUBJECT)

(Bucky and Screens)

Film	Tube	T.F.D.	Anode	Ma.	K.V.P.	Sec.
1	6 K.W.	25	To Head	10	78	10
2	6 K.W.	25	To Feet	10	78	10
53	5/10 10/64	25		10	78	10
54	3 K.W.	25	To Feet	10	78	10
58	3 K.W.	25	To Left	10	78	10
55	3 K.W.	30	To Feet	10	86	10
56	5/10 10/64	30		10	86	10
57	3 K.W.	30	To Left	10	86	10

PELVIS (LIVING SUBJECT)

(Bucky, No Screens)

66	3 K.W.	25		10	88	20
67	3 K.W.	25		10	88	30
68	6 K.W.	25		10	88	30
69	5/10 8/64	25		10	88	30
70	5/10 10/64	25		10	88	30
71	5/30	25		10	88	30

LATERAL SPINE

(Bucky and Screens)

59	3 K.W.	25	To Feet	30	88	10
60	3 K.W.	25	To Back	30	88	10
61	5/10 10/64	25		20	88	15
80	5/10 8/64	25		10	90	30
81	3 K.W.	25	To Back	30	91	10
82	6 K.W.	25	To Back	60	90	5

EXAMINATION OF SMALL AREAS

If it is desired to examine small areas, and it is necessary to use large amounts of energy in order to make quick exposures, it would seem that better detail of structure should be obtained if the Philips type of tube were used.

For this comparison, the mastoids, lateral heads, and paranasal sinuses were observed.

TABLE IV

LATERAL HEAD

(No Bucky)

Film	Tube	T.F.D.	Ma.	K.V.P.	Sec.
117	3 K.W.	25	100	85	1/2
118	5/30	25	100	85	1/2
119	5/100	25	100	85	1/2

PARANASAL SINUSES

(No Bucky)

120	5/100	25	100	88	3/10
121	6 K.W.	25	100	88	3/10
122	6 K.W.	28	100	70	2
123	5/100	28	100	70	2
124	5/30	28	50	76	5
125	3 K.W.	28	50	76	5
126	5/10	28	10	75	10
127	5/10	28	10	75	10
128	3 K.W.	28	10	75	10

PARANASAL SINUSES

(Bucky)

129	3 K.W.	25	10	85	10
130	5/10	25	10	85	10
131	5/10	25	10	85	10
132	3 K.W.	25	10	85	10

LATERAL HEAD

(Bucky)

133	3 K.W.	25	10	80	5
134	5/10	25	10	80	5

MASTOIDS

110	5/100	18	100	83	1/10
111	3 K.W.	18	100	83	1/10
112	3 K.W.	24	100	90	1/10
113	5/30	24	100	90	1/10
114	5/100	24	100	90	1/10
115	3 K.W.	24	100	77½	3/10
116	5/30	24	100	77½	3/10
142	3 K.W.	24	100	70	1/2
143	5/30	22½	100	70	1/2
144	5/30	24	100	70	1/2

Film No. 112, of the mastoid, was made with the 3 K.W. Philips tube in 1/10 of a second at a 24-inch target film distance, and Film No. 113 was made with the 5-30 Coolidge tube, using the same factors. There is no difference in the detail of the structure

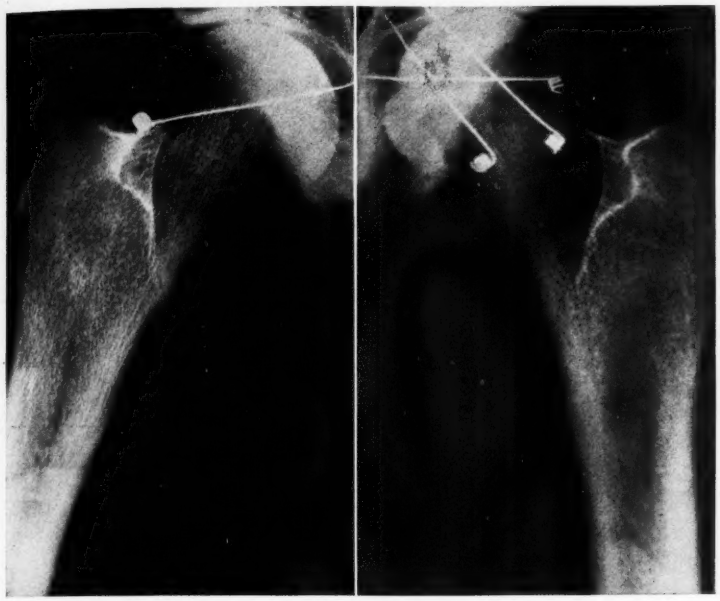

Fig. 6, Film No. 90. A 14 × 17 in. film of dried pelvis. Contact prints of femurs to show the difference in detail of structure. Anode of the 3 K.W. Müller Metalix tube toward the left. The detail is good as if a fine focal spot tube were used. On the opposite side of the film, the right hip shows blurred detail, as if made by a broad focal spot tube. This demonstrates the effect upon detail when a rectangular focal spot tube is used.

of the mastoid in either film. Between Figure 9, Film No. 115, made with the 3 K.W. Philips tube, and Figure 10, Film No. 116, made with the 5-30 Coolidge tube, using 3/10 of a second, there is no difference in the detail of the mastoid process, and very little difference in contrast. There is improvement of contrast, when compared with the film made in 1/10 of a second.

The same is true in the films made of the lateral heads and paranasal sinuses. The reason for this lies in the fact that the parts examined were close to the film, and when structures can be so placed, the size of the focal spot does not play so important a part in showing the sharpness of detail.

In referring to Table IV, it will be observed that the factors used were larger amounts for both current and voltages than are rated for the tubes, but as the time of exposure was very short, it did not appear to damage the tubes when they were energized with current rectified by the double cross arm type of rectifying switch.

In the study of the lateral spine, because the vertebræ form a narrow line, it was thought that by placing the Philips tube with the anode toward the back, so that it was centered over the bodies of the vertebræ, the rays corresponding to those that produce the sharpest lines, as demonstrated by the wire mesh films, would pass through the vertebral column and bring out more detail of structure than could be obtained with the Coolidge tube. The films made with both types of tube demonstrated, however, that the detail was equal in the films made with the two types of tubes, so that nothing was gained by using a Philips tube, except that more energy could be used in that tube and the time of exposure shortened.

Fig. 7, Film No. 83. Made of dried specimen with 5-10 Radiator type Coolidge tube. See text for description.

Fig. 9, Film No. 115. Mastoid made with 3 K.W. Müller Metalix tube. See text.

INCREASE IN TARGET FILM DISTANCE

Because the detail of the structure is more evenly distributed over the film with the Philips tube when the target film distance is increased, it was thought that by using this tube in the examination of the chest, more of the detail of the lung structure might be shown on the film.

Fig. 8, Film No. 83. Contact films of femurs from 14 × 17 in. film made with a 5-10 Coolidge tube. Note the uniformity of detail in all directions. This detail cannot be reproduced when using a 3 K.W. Philips type of Müller Metalix tube. (Compare with Figure 7.)

TABLE V

LUNGS AND HEART

48 inches T.F.D.

Film	Tube Anode	Ma.	K.V.P.	Sec.
72	3 K.W. A. to right	100	83	1/10
73	6 K.W. A. to head	100	83	1/10
75	5/30	100	83	1/10
76	5/100	100	83	1/10
77A	5/100	350	60	2/10
141	5/30	100	90	1/20
145	5/30	100	83	1/10
146	3 K.W. A. to left	100	83	1/10

84 inches T.F.D.

74	6 K.W. A. to head	100	115	1/10
77	5/100	100	115	1/10
78	B.F.U.	350	B25	1/20
79	B.F.U.	350	B25	1/10

TABLE VI

FETUS

(Bucky and Screens)

Film	Tube	T.F.D.	Ma.	K.V.P.	Sec.
146A	5/30	30	40	88	8
147	3 K.W.	30	40	88	8
148	3 K.W.	30	40	88	8
149	5/30	30	40	88	8

GALL BLADDER

(Bucky)

151	5/30	30	50	75	2
152	3 K.W.	30	100	80	1/2
153	5/100	30	100	80	1/2
154	5/100	30	100	80	1/2
155	3 K.W.	30	100	80	1/2
156	5/30	30	100	80	1/2
157	5/30	30	100	67	1 1/2
158	3 K.W.	30	100	67	1 1/2
159	5/100	25	100	67	1
160	5/100	30	100	67	1 1/2

In Figure 11, Film No. 145, and Figure 12, Film No. 146, made with a 5–30 Coolidge and a 3 K.W. Philips tube, respectively, no difference in detail could be noted. In the films made at 84 inches target film distance, the best film was No. 79, made with the B. F. Universal Coolidge tube in 1/10 of a second, using 350 ma. of current. This was because of the improvement in contrast, making detail more visible, the actual detail being the same in this group of films. (See Table V.)

Fig. 10, Film No. 116. Same mastoid as shown in Figure 9, made with 5-30 Coolidge tube. See text. When a small area, located near the film, is examined there is no difference noticeable between films made with Coolidge or Müller tube. (See Figure 9.)

In the examination of the gall bladder, detail is not necessary and contrast is more important, so that a fine focal spot tube is not needed, but larger amounts of current and shorter time for exposure are more desirable. The 5–100 Coolidge tube meets this requirement, and, for some reason, the films made with this tube were better in the gall-bladder group than those made with the Philips tube.

In the fetus group, there was no difference in the films made with either tube.

DISCUSSION

The construction of the Philips type of Müller Metalix tube, by the elongation of the focal spot to carry larger amounts of energy, and the geometry, to compensate for the rectangular shape of the focal spots, make the tubes unsatisfactory where detail

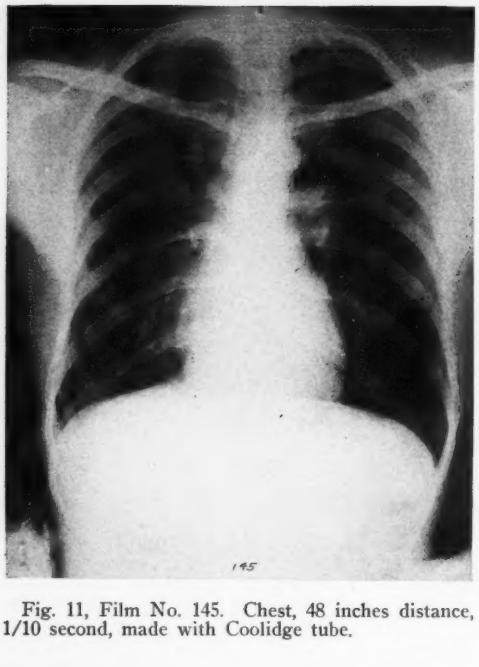

Fig. 11, Film No. 145. Chest, 48 inches distance, 1/10 second, made with Coolidge tube.

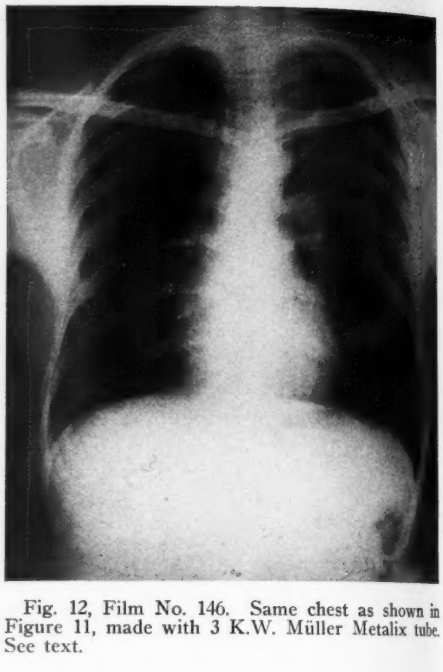

Fig. 12, Film No. 146. Same chest as shown in Figure 11, made with 3 K.W. Müller Metalix tube. See text.

is important over a large area, as in the examination of the bony pelvis. For this class of work much better films are obtainable by using the Coolidge tube, and, as speed in exposure time is not usually necessary, the finest focal spot Coolidge tube may be used, and this gives much sharper detail of structure than the 3 K.W. radiator type Philips tube.

Where small areas were examined, there was no difference in detail on the films, whether made by the Coolidge or Philips tubes, and the speed of exposures, as recorded in the tables, is rapid enough to meet the usual requirements. Therefore, no advantage was gained by using the Philips tube.

SUMMARY

After a thorough investigation, the conclusions are: In the examination of small areas, the detail of structure was no sharper on films made with the Philips tube than on those made with the Coolidge tube. Films were made of each patient with both types of tubes.

Furthermore, when large areas are examined, where detail is important, the films made with the Coolidge tubes show sharper and uniform distribution of detail, while those made with the Philips tube show distorted and variable detail in various parts of the films.

THE MEASUREMENT OF X-RAY DOSAGE BY PHYSICAL MEANS[1]

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THE life course of a cell depends on the internal conditions of the cell and on the medium in which it happens to be. The marked changes which X-rays are capable of producing in a living cell may be due to the direct action of the radiation on the cell itself, or a primary action on the medium, which then influences the cell, or to a combination of the two. Whatever the actual mechanism may be, the resultant effect is related in some way to the radiation which causes it. The establishment of this relation between cause and effect under various conditions is of utmost importance, but, unfortunately, it is a very difficult problem. In the first place, no relation can be established unless we are able to measure definitely both the cause and the effect. That this is not a simple matter is but too well known. In the present paper we shall limit our discussion solely to the measurement of the causative agent, X-radiation.

If the action is simply a direct one on the individual cell, the only radiation which can influence it is the radiation which reaches it. Furthermore, in view of the great penetrating power of the type of radiation under discussion, only a small part of the radiation which reaches a cell can have any influence on it: that is, only the fraction which is absorbed by the cell is responsible for the changes which may be produced. The same mode of reasoning applies, *mutatis mutandis,* to the medium, if the action on the cell is assumed to be an indirect one. In other words, the medium can be modified only by the radiation which it absorbs. We may conclude, therefore, that in any case the factor which is *directly* responsible for the observed changes is the part of the radiation which is absorbed by the tissue.

If we study the passage of X-rays through matter we find that it is a very complicated process. We cannot determine with any degree of definiteness just how much radiation which is biologically effective at volume of tissue irradiated under specified conditions. The chief difficulty is due to the fact that radiation is scattered repeatedly during its passage through matter, and its quality is altered both by true absorption and scattering. Accordingly we are not in a position to determine accurately the factor which in the ultimate analysis must be directly responsible for the biological change. There is also a subsequent difficulty: if we know the amount of radiation actually absorbed per unit volume of the irradiated tissue, we still do not know whether this is *all* biologically effective; or, *what is more important,* whether the fraction which is biologically effective is always the same, irrespective of the wave length. In view of these difficulties, it is evident that, for the present, at least, we cannot correlate cause and effect (radiation and biological change) *in the most direct way.*

From the preceding discussion it is apparent that the ideal method of dosage would be based on the measurement of the radiation which is biologically effective at every point in the irradiated tissue. The "dose of radiation" would then express the part of the radiation which reaches a certain point in the tissues in terms of its biological effectiveness with regard to the particular biological change we wish to produce. Since this is impossible at present, we must find some indirect method to fulfill our im-

[1]Read before the Radiological Society of North America at the Fourteenth Annual Meeting, at Chicago, Dec. 3–7, 1928.

mediate requirements. We may even limit our requirements to the following: (1) duplication of treatments in the same radiological clinic, and (2) comparison of treatments given in different clinics.

Let us consider first the question of duplication of treatments. For a single treatment the biologically effective radiation at any point in the tissue depends on (1) the intensity of radiation, (2) the duration of the continuous irradiation, (3) the quality of the radiation. Therefore, in order to duplicate treatments we must at least duplicate these three factors "at every point." While this is sufficient in the case of superficial therapy (points on the skin, and soft rays), an additional factor must be considered in the case of "deep therapy." That is, if two tumors are at different depths from the skin, the criterion for duplication of treatments cannot be the duplication of the above three factors at every point from the skin downward, because then points within the two tumors would not receive the same amounts of biologically effective radiation. In this case we are not even sure that duplication can be obtained by having the same distribution of radiation within the two tumor masses, since the effectiveness of the radiation may depend on its distribution in surrounding tissues. Aside from this theoretical difficulty we have practical difficulties which make it impossible for us to measure actually the intensity and quality of radiation at every point in the tissue. We find, therefore, that the duplication of treatments by the duplication of the three factors stated above is not possible at present. Let us, therefore, look for indirect means.

The intensity of radiation at any point in the neighborhood of a Coolidge tube depends, in general, on: (1) the magnitude of the applied voltage; (2) the nature of the applied voltage (whether fluctuating, constant, or otherwise); (3) the electron current from the cathode to the anode; (4) the phase relation between voltage and current; (5) the construction of the tube, particularly as regards the material of the target; (6) the material between the target and the point in question (gas-tight envelope, filter, and tissue); (7) the presence of other scattering material, its composition, size, and relative position; (8) the distance from the focal spot to the point; (9) the orientation of the point with respect to the target; (10) the presence, size, and relative position of diaphragms and screens. While some of these factors are more important than others, it is still necessary that they shall all be specified in order to duplicate in general the intensity of radiation at any point. Fortunately the factors which control the quality of radiation are all included above, but nevertheless we have a formidable number of variables with which to deal.

Some of these variables are not easily controllable, and among these are the most important ones. The spark gap and milliammeter, which are the only instruments available to most radiologists, are utterly insufficient. To prove this it is only necessary to relate a personal experience: A new synchronous motor was installed in one of our X-ray machines. This necessitated resetting the rectifying switch. The work was done by the concern from which the machine was originally purchased, and the apparatus was turned over to us as "ready for use." Upon testing the X-ray output, we found that it was just 50 per cent of the original value, although the *spark gap* and *milliammeter* readings were the same as before the repairs were made. The discrepancy was due to improper setting of the rectifying switch. After correcting this the X-ray output was brought up to normal. This, of course, is an extreme case, but many smaller variations may occur which cannot be detected by the spark gap and milliammeter. To control individually some of the factors listed above, very complicated apparatus

would have to be used; hence we may conclude that the accurate determination of the radiation intensity by such means is impractical.

In our discussion so far we have seen that we cannot determine accurately the biologically effective radiation at a point within the irradiated tissue, either directly or indirectly. How, then, can we duplicate treatments? The answer is that, unless we impose certain restrictions or make certain assumptions, we cannot do so. If the spark gap and milliammeter are the only two measuring instruments at our disposal, the restrictions are so numerous that the field becomes extremely narrow. Under these conditions it is possible to duplicate surface doses in the same clinic, using the same apparatus, by maintaining all the treatment factors constant. That is, the spark gap, the milliamperage, the filter, the distance, and the size of the field must be always the same. But this is true *only so long as no changes occur* in the apparatus and measuring instruments. Since changes are apt to occur, and at least some can not be detected by the spark gap and the milliammeter, it is evident that duplication of doses can not be relied upon over a reasonable length of time, even with the restrictions mentioned above. *A fortiori,* treatments given in different clinics can not be compared. What additional equipment will enable us to do these things without too many restrictions?

Without giving elaborate details we may say that an instrument which is capable of giving an indication of the intensity of radiation and its quality will simplify the problem very considerably. At the present time there are on the market many such instruments, all of which have their merits and their faults. Most of them are ionization instruments, which measure the ionization produced by X-rays in a certain volume of air. They consist of two essential parts, which in some instances are combined in one: (1) the ionization chamber in which the air is ionized by the rays reaching it, and (2) the electrical device for the measurement of the ionization current. In the following paragraphs we shall endeavor to bring out the range of usefulness and the limitations of these instruments in general.

We may mention, first, that no practical ionization instrument measures the *intensity of radiation.* In physics the intensity of radiation at a given point may be defined as the amount of energy passing per second through an area of one square centimeter placed at the point in question perpendicular to the line of propagation. The ionization instrument measures only a fraction of the energy flux, and *not always the same fraction.* This, in particular, is what causes trouble. The degree of ionization in the instrument does not depend only on the intensity of the radiation but also, and to a marked degree, on the wave length. Accordingly, beams of different wave length which give the same ionization reading have not the same intensity of radiation in the physical sense. Furthermore, two beams which give the same readings with one ionization instrument may not give the same readings with another instrument of different construction.

The fact that ionization instruments do not measure the true intensity of radiation irrespective of the wave length is not of particular significance for purposes of dosage. As already pointed out, we are interested here in the fraction of the total radiation reaching a tissue, which is biologically effective. The ionization instrument measures the fraction of the total radiation which is effective in producing ions in the particular ionization chamber employed. Neglecting for the moment that this depends on the construction of the chamber, we may ask whether there is any simple connection between the radiation which is effective in producing ions and that which

is effective in producing a biological change, irrespective of the wave length. This question has been discussed extensively in the literature for a number of years, but no clear-cut answer is to be found. Many carefully worked out experiments have been reported, but the results are contradictory. In our estimation the discrepancies are due to differences in the construction of the ionization chambers and differences in the biological materials employed in the experiments.

In recent years we have heard a great deal about ionization chambers which give readings "independent of the wave length." If this "independence" is determined by comparison with the so-called open air ionization chamber, it simply means that the two ionization chambers give proportional readings, irrespective of the wave length. However, the real question is whether there is proportionality between such ionization readings and biological effects, irrespective of the wave length. This point, as already stated, has not so far been settled. It is not wise, therefore, to rely blindly on such chambers for the determination of doses to be administered to patients under widely different conditions of voltage and filtration. Human tissues are far too complex to follow any simple relation in their reaction to radiation. We may mention in this connection the results obtained by Mrs. Quimby when using, successively, rays of different quality to produce a skin erythema. Mrs. Quimby is reading a paper on this work at this meeting and therefore we need not give the details here. Briefly stated, she determined by skin tests on patients the dose which would produce a threshold erythema, using X-rays and gamma rays separately. Then tests were made with 50 per cent of the X-ray dose, followed immediately by 50 per cent of the gamma ray dose (or *vice versa*), and no visible skin changes were produced. In order to get the same threshold erythema as with either type of radiation alone, about 30 per cent more of the combined radiation had to be used. The explanation of this result is rather difficult, but it is certain that no ionization measurements could predict it.

At this point it may be well to examine a little further the question of independence of wave length in ionization measurements. As already stated, the criterion for this is comparison of readings with an "open air" ionization chamber. The question of proportionality between such readings and the biological effectiveness of the radiation is still unsettled. Nevertheless, it is important to note that an ionization chamber which fulfills this requirement is much more apt to give us a measure of the biologically effective radiation. This is due to the fact that the laws which govern the passage of radiation through matter (true absorption, scattering, etc.) depend on the atomic composition of the material. Accordingly, an ionization chamber made up of materials whose atomic numbers are very close to those of tissue constituents, will modify the radiation which traverses it in essentially the same way as tissue. On this account it is reasonable to expect a more direct relation between ionization readings obtained with such a chamber and biological effects. However, it does not necessarily follow that this relation should be one of simple parallelism for all wave lengths and all biological effects.

From the preceding discussion it is evident that, in general, an ionization chamber of the type just described is much to be preferred for dosage purposes. However, we should always bear in mind that a direct parallelism between the radiation which is effective in producing ionization *even in this chamber,* and the radiation which is effective in producing a biological change, has not been definitely established. In this connection it may be of interest to indicate a

practical result which would follow if such a parallelism did exist. Many determinations of the distribution of radiation at different tissue depths have been made. In most cases, small ionization chambers made of light materials have been used. It has been found that the *relative* amount of radiation reaching a depth of 10 cm. is considerably greater in the case of high voltage X-rays, as ordinarily used in therapy, than in the case of gamma rays, where practical considerations limit the distance of the radium from the skin to approximately 10 centimeters. Assuming that the ionization chamber measures the biological effectiveness of radiation, it must follow that a deep-seated tumor can be treated better by X-rays. Still, radium in large amounts is being used more and more for external irradiations. Those who have had most experience with this method, believe that better results are obtained with "long distance" radium treatments than with high voltage X-rays. If this be correct, we must conclude that a "smaller" dose of gamma rays is biologically more effective than a "larger" dose of X-rays in the case of deep-seated tumors. Or, from a different point of view, the ionization chamber measures a *smaller* fraction of the biologically effective radiation at a tissue depth of several centimeters, in the case of gamma rays than in the case of X-rays. This is not at all impossible, if we remember that the quality of the radiation is modified considerably in its passage through tissues. However, in view of the many practical difficulties in comparing clinical results and the difference in other factors, besides the relative depth doses in the two types of treatment, no very definite conclusions can be reached.

We have pointed out that the spark gap and milliammeter are insufficient for the duplication of treatments. We then mentioned that an ionization instrument is of great help for this purpose, and we came to the conclusion that, in general, it is preferable to have an ionization chamber which shows a parallel relation with an open air chamber for different wave lengths. We shall now discuss how an ionization instrument can be used to best advantage for practical purposes.

It was stated earlier in this paper that in the same clinic, using the same apparatus, surface doses could be duplicated by means of the spark gap and milliammeter, *provided no changes occur in the apparatus and measuring instruments.* By means of an ionization instrument, it is possible to determine when changes of appreciable magnitude have occurred. The desirability of its use is therefore apparent. How should such an instrument be constructed, and how used? For the present purpose, *i.e.,* duplication of surface doses with the same apparatus, the construction of the ionization chamber is of no importance. All we want to know is that the emission of X-rays remains constant when the spark gap and milliammeter readings are the same. The ionization chamber may be small or large, may be portable or attached to the X-ray tube holder. In the latter case, if it is in the path of the useful beam, the walls of the chamber should be such as to offer a negligible absorption to the passage of the rays. The radiologist is not limited to any set of conditions in the duplication of treatments. He can, for instance, use any target skin distance, or any filter. It is necessary, however, that in duplicating to-day a treatment he gave two weeks ago, he use again the same treatment factors (voltage, current, filter, distance, field, etc.), making sure that the ionization reading is substantially the same as before. In spite of obvious limitations, the radiologist now is not completely at the mercy of his apparatus. In practice absolute duplication is not necessary, and small errors may be neglected. With this proviso we can extend the usefulness of the

ionization instrument considerably, by imposing some restrictions on the construction of the chamber.

Let us assume, therefore, that the chamber is made of organic materials and that it offers little resistance to the passage of radiation. We can now compare the output of X-ray machines of different construction running at the same voltage. It is known that machines of the mechanical rectifier type produce radiation which may differ both in intensity and quality. Also, the output of the same machine varies according to the rectifier setting and other conditions. However, such variations, in general, are not very large. With an ionization chamber made of organic materials the difference in quality for the same applied voltage and filter would not be large enough to be significant. Accordingly, the readings may be assumed to be proportional to the biologically effective radiation. If the possibility of a larger error is borne in mind, comparisons may also be made with voltages and filters which differ to some extent. The greater these differences are, the greater the possible error. When voltages and filters are quite different, it is necessary to proceed with great caution and to rely more and more on the empirical determination of dosage, using the ionization readings simply as a guide.

So far we have referred to "surface dosage": when we come to *"depth dosage"*[2] the problem becomes more complex. We have already mentioned the fundamental difficulty as to what constitutes equality of treatment in the case of two tumors, which are at different depths from the skin. Our present knowledge does not permit us to overcome this obstacle. We may, however, limit the comparison to doses at the same tissue depth.

No matter how the ionization chamber is made, it is not possible to place it within the irradiated tissue of the patient to determine the distribution of the radiation. Hence it is necessary to obtain this information by indirect means. A water phantom (or wax blocks) and a very small ionization chamber are generally used for this purpose. The small ionization chamber is essential in this case, and, therefore, the measuring instrument must be very sensitive. Such instruments are subject to numerous disturbances and are, therefore, not adapted to be used in the radiological clinic. Furthermore, the indirect determination of depth doses can be carried out to better advantage in the experimental laboratory. The results can be made available in the form of charts or tables.

When the radiologist makes use of these he should bear in mind some important factors. In the first place, the data were obtained under definite experimental conditions (voltage, filter, field, size of phantom, etc.). If the clinical conditions are not essentially the same, the data are not applicable. In particular we may mention the influence of the size of the irradiated volume, which is often left out of account. If the depth distribution of radiation is determined in a large phantom, using a large field, the results are not applicable, for instance, to the treatment of a wrist, where the irradiated volume is much smaller. In this case the radiologist should "build up" the patient's wrist to approximately the size of the phantom employed in determining the depth doses, in order to obtain comparable conditions. This building up can be done by means of paraffin blocks, water bags, etc. In any case, it should be remembered that depth doses can only be approximated, because the patient's body is not a solid mass of homogeneous tissue, but has air cavities and bones which may influence the distribution of radiation to a considerable extent. This being the case, the determination of depth doses in the radiological clinic is hardly justified, except perhaps where an attempt

[2]These expressions are used here metonymically in accordance with common practice.

is made to reproduce experimentally the part of the patient's body to be treated.

Another point to bear in mind is the possibility of a fundamental error in all depth dose determinations, due to the change in quality of the radiation with the tissue depth. This is not important provided the voltage and filter are not varied considerably, but it may be significant when treatments with rays of essentially different quality are compared. (The case of high voltage X-rays and gamma rays has already been discussed from this point of view.)

Accepting the proposition that it is preferable for the radiologist to apply to his needs data on depth doses obtained in the experimental laboratory, it follows that he does not need a *small* ionization chamber for this purpose. Does he need one for other practical purposes? The answer, of course, depends on what he wishes to do, but we feel that he may very well dispense with it. In addition to the determination of depth doses, there are two other instances where a *small* ionization chamber is essential: The determination of surface doses for different target-skin distances, or different field areas.[3] For the same reasons which led us to recommend that depth doses be determined under proper conditions in the experimental laboratory, we reach the same conclusion here. Tables and curves can be worked out to meet all practical requirements. Some are already available. In the case of the target-skin distance a first approximation may be obtained by using the inverse square relation, since in practice doses determined in this manner do not differ greatly from the actual doses.

To summarize our ideas on ionization instruments expressed so far, we may say that: (1) such an instrument is indispensable to the radiologist; (2) the ionization chamber should be made of organic materials, and should absorb little radiation; (3) it need not be a small one such as is used for the determination of depth doses. We feel that a rather large ionization chamber is preferable for practical work in the clinic, for many reasons: (1) the electrical measuring instrument need not be so sensitive, and therefore it is less subject to variations due to extraneous causes; (2) the large chamber is less fragile than a very small one; (3) it can be permanently attached to the X-ray tube holder without impairing its usefulness; (4) it is less apt to be misused, since the radiologist knows definitely that it gives him only a measure of the radiation emission, and not the "dose"; (5) the radiologist must consider separately all the factors which determine the dose; (6) finally, the tyro in radiology is not led to believe that all he needs to treat patients with X-rays is a small ionization chamber which gives him the "dose administered."

The addition of an ionization measuring instrument to the equipment of the radiological clinic is of great advantage. But, of course, any piece of apparatus may go out of order at any time. If it stops functioning, in general, no harm results aside from the expense and inconvenience caused by the repairs. On the other hand, if the calibration of the instrument changes and the change is not apparent, considerable harm may be done. This depends on how much the radiologist relies on the particular instrument. To overcome this difficulty it should be possible for the radiologist to check all his instruments from time to time.

Modern practice recommends the use of two milliammeters to measure the electron current through the tube. Following this procedure, a change in the calibration of the meters is more apt to be discovered, since it is unlikely that both would change in the same way. It is preferable, and not less convenient, to have two milliammeters permanently connected, but to have only one in operation. The other should be short-cir-

[3] In this may be included the variation of the depth of the irradiated volume.

cuited by a simple switch which can be opened whenever it is desired to check the first meter. This should be done periodically.

The spark gap reading is subject to variations due to changes in the instrument proper (change of shape, dirt, etc.), and to changes in atmospheric conditions. It is preferable not to use the spark gap every day, but to calibrate the voltmeter across the primary of the transformer and then set the machine according to the readings of this meter. The calibration can be made some day when weather conditions are satisfactory. While this is being done, it is necessary that the same tube current be used as for the actual treatments. A reserve voltmeter may be used to check the one in constant use, but, in addition, check readings with the spark gap should be taken from time to time.

In the case of the ionization instrument, the same control of its calibration is necessary. If two are available they should be checked against each other from time to time. With these instruments, however, it is more likely that considerable changes in calibration occur. Accordingly it is very desirable that each be provided with suitable means for rapid calibration before (and sometimes after) it is used. Such calibration is best made by means of a radio-active material whose radiation remains practically constant over a period of years.

The interdependence among the readings of the three instruments just mentioned, makes possible a check on the third by the readings of the other two. Thus, if the primary voltmeter and the milliammeter read the same as previously, but the ionization instrument shows a different reading, something has gone wrong. Similarly, if the milliammeter and the ionization instrument give their normal readings, the primary voltmeter should do so also. In practice it is sometimes impossible to duplicate all readings on account of line voltage variations. This is really due to the fact that most X-ray machines are not equipped with a fine voltage control to make adjustments between the more or less coarse steps of the autotransformer and rheostat. In this case the voltage can be set to the nearest step on the control and the proper allowance for the difference in X-ray emission can be made by the ionization measurement. It may be well to mention here that in general the X-ray emission is influenced to a certain extent by the relative settings of autotransformer and rheostat, even though the applied voltage has the same value. It is desirable, therefore, to reproduce as closely as possible the same autotransformer and rheostat settings whenever the machine is used after calibration with definite settings. The ionization instrument, of course, will indicate any variation due to this cause.

The addition of an ionization instrument to our radiological armamentarium makes possible, within certain limits, the duplication of X-ray treatments in a given clinic. In order to compare treatments administered in different clinics, no additional apparatus is needed, but it is essential that the instruments used in the different clinics meet certain minimum requirements, and be calibrated by comparison with a standard, under the conditions in which they are to be used. To facilitate this, the definition of a unit of X-radiation has been agreed upon at the recent International Congress of Radiology. It is as follows: "The International Unit (of X-radiation) is the quantity of X-radiation which, when the secondary electrons are fully utilized and the wall effect of the chamber is avoided, produces in one cubic centimeter of atmospheric air at 0° Centigrade and 76 cm. mercury pressure, such a degree of conductivity that one electrostatic unit of charge is measured at saturation current." Unfortunately, however, no definite instrument has been chosen to establish this unit experimentally. We have, therefore, no final standard of reference with which other instruments may be compared.

The radiologist knows that the word definition of a unit is of no value to him in his daily work. He may, therefore, wonder why no international standard has been adopted, when so many instruments purporting to measure "doses" in roentgen units are already on the market. The word "doses" is put in quotation marks by the writer because the International Unit is not a unit of dose, but "a unit of X-radiation," involving a certain quantity of X-radiation. This is one factor which determines the dose, but not the only one. The reason for not adopting a standard instrument at this time is that the problem is much more complex than it appears on the surface, and it has not been solved satisfactorily.

If to-day we had no standard of length it would be a simple matter, technically speaking, to take a certain rod (of platinum-iridium) and agree to call that the unit of length. There would be no trouble in making other rods of the same length and using them as secondary standards. This is because we all know what is meant by length, and we can all visualize it. But "quantity of X-radiation" is not a familiar concept and the matter is further complicated by the implicit definition of this attribute of radiation in the definition of the unit. That is, "quantity of radiation" in the definition is really determined by the ionizing power of the radiation *under specified conditions*. It is not the "amount of radiant energy," which is inherently independent of method and apparatus.

It would be possible at the present time to adopt as standard any one of several instruments and to calibrate secondary standards by comparison with it under specified conditions. These conditions, however, would be more or less arbitrary. The chief difficulty is that we do not know just what system of diaphragms should be used to make sure that we are measuring the thing we want to measure, or always the same fraction thereof. Neglecting possible experimental errors, this is probably the reason for the disagreement among readings taken of the same beam of radiation with different so-called standard instruments. The discrepancies can be very considerable because the adoption of a certain system of diaphragms by one investigator is now largely a matter of personal opinion. If we all adopt the same system of diaphragms for the purpose of standardization, there will be no discrepancies among the different instruments due to this cause. But in radiological practice we cannot use the same system of diaphragms, and therefore we may introduce an error of unknown magnitude which varies with the sizes and positions of the diaphragms actually used. For these reasons we feel that the agreement among different instruments reported by some investigators is more or less accidental and in any case it is not significant.

In view of this situation the general use of the International Roentgen Unit in the radiological clinic is impossible at present. It may be used by that name in some hospitals where "standard" instruments have been developed, and each hospital may claim that its unit actually represents the International Roentgen Unit. But there can be no uniformity, general agreement, and real significance in the measurements until an actual standard instrument is set up and the proper standard experimental procedure is worked out. When this has been done by our National Bureau of Standards we shall have in this country the proper conditions for the use of at least a national unit.

In the meantime it may be well to remember that a dose of radiation can never be expressed by a *single* factor. As already stated, the roentgen unit is not a unit of dose but a unit of something which is related to the quantity of radiation. But even this must be taken in a restricted sense. For

instance, let us consider two skin treatments with fields of 25 and 100 sq. cm., respectively. If the *total* quantity of radiation administered in the two cases is the same, the intensity or "density" factor will be about four times larger in the case of the smaller field. The density factor unquestionably has a more important influence on the biological effects, but the total quantity is not without importance. Usually no mention is made of this except indirectly by stating the size of the field, and the factor which is expressed in roentgen units refers to one square centimeter of surface.

In addition to these factors at least two others of great importance must be stated in order to specify a dose of radiation with any degree of completeness. They are the quality of the radiation used and the duration of the continuous irradiation. The latter, of course, offers no practical difficulties. On the other hand, no simple method has been worked out for the specification of radiation quality and no general agreement has been reached as to the best practical method available at present. The International X-ray Unit Committee made the following recommendation at the Second International Congress of Radiology: "That any specification of dosage is incomplete without specifying the quality as well as the quantity of the radiation. The quality of the X-radiation used for practical purposes varies widely and it would be impractical to give a complete specification of it, but much information can be obtained from a knowledge of the degree of absorption of the radiation in standard materials, the peak voltage applied to the tube, together with the filter employed, and the general character of the high tension apparatus. For practical purposes the quality may be expressed by stating the half-value layer in a suitable material, or by stating the effective wave length as determined by the percentage amount of radiation transmitted through a given thickness of a suitable material (copper or aluminium)."

It will be noted that this leaves considerable latitude in the choice of a method. Furthermore, the last recommendation is rather ambiguous, assuming that it was not the intention of the Committee to suggest that specification of either the half-value layer or the effective wave length is fully sufficient for practical purposes. The work of Mrs. Quimby[4] bearing on this problem proves beyond any doubt that the quality of radiation cannot be specified by a single factor, whether this be the half-value layer, the absorption coefficient, or the effective wave length. This is evident when we consider that Mrs. Quimby obtained experimentally beams of radiation having the same half-value layer, or the same absorption coefficient, or the same effective wave length, with voltages ranging from 125 to 200 K.V. by a suitable choice of filter. For instance, with the particular machine used, the following combinations of voltage and filter gave the same effective wave length, calculated according to Duane's method: (1) 200 K.V., 0.20 mm. Cu.; (2) 175 K.V., 0.28 mm. Cu.; (3) 150 K.V., 0.46 mm. Cu.; (4) 125 K.V., 0.76 mm. Cu. If, however, we include additional factors mentioned in the Committee's report, we can specify the quality of radiation with sufficient accuracy for practical purposes. They are: the general character of the high tension apparatus, the peak voltage applied to the tube, and the filter.

To determine the half-value layer, the absorption coefficient, or the effective wave length, a measuring device is necessary. The same instrument which is used for the determination of the intensity factor of a dose may be utilized for this purpose. It should be noted, however, that the values obtained for these factors are dependent to a certain extent on the particular instrument

[4] A paper on this subject will appear soon in the *American Journal of Roentgenology and Radium Therapy.*

and experimental procedure employed. In the absence of a universal agreement on these matters, it is desirable that the essential experimental conditions be stated.

In conclusion, we may say that the specification of an X-ray treatment should include: (1) A description of the part treated (shape and size of tumor, depth below skin, etc.); (2) the general character of the X-ray machine and tube; (3) the peak voltage and how determined; (4) the filter (consisting of whatever may be between the tube and the patient along the useful beam); (5) the target-skin distance, the shape and size of the field; (6) the arrangement of the fields and directions of the beams; (7) the duration of each irradiation; (8) the interval between successive irradiations, and total number given. If a "calibrated" ionization instrument is available, we should add (9) the intensity factor of each irradiation expressed in roentgen units per second, and (10) the effective wave length (or the absorption coefficient or the half-value layer), stating how it was determined. These ten factors are essential in order to convey a comprehensive idea of a treatment.

SUMMARY

1. Progressive development of radiation therapy requires the proper correlation of *cause* and *effect*. In the ultimate analysis this means the establishment of definite relations between the radiation used and the clinical results obtained. To do this we must have, in the first place, an accurate knowledge of the radiation which is effective in producing the observed results. It is not sufficient to have a knowledge, however complete, of the radiation emitted by the particular source at our command.

2. Since we do not know just how radiation is biologically effective, it is very desirable that we shall have clearly in mind at all times all the factors which may possibly influence the biological changes produced by the radiation.

3. We must think of a dose of radiation as that which is directly responsible for the observed biological change. Since the change takes place in a biological medium, the important thing is the dose at every point of the medium. This cannot be measured by a physical instrument.

4. The dose of radiation at a given point in the medium involves three distinct factors: (*a*) the *effective* intensity, (*b*) the duration, and (*c*) the quality. Of these only the second is the same at every point and can be measured. The first and the third can be determined only approximately and by indirect means.

5. The writer is of the opinion that the radiologist should not attempt to estimate experimentally the effective intensity and the quality of the radiation *within the irradiated volume*. Work of this sort can be carried out best in the experimental laboratory under the proper conditions. He should have, however, a sufficient knowledge of such work to appreciate the assumptions and approximations involved in the data which is made available to him by the research laboratory.

6. The determination of radiation doses at the point of entry of the useful beam (surface of the skin) is a relatively simple matter; nevertheless, there is a serious difficulty due to the radiation which is scattered by the medium. This radiation on the average is softer than the primary radiation and, therefore, may have a different degree of biological effectiveness. The evaluation of the relative amounts of scattered radiation under different conditions is also a problem to be investigated in the research laboratory.

7. In view of the foregoing considerations, for the present we may dismiss the idea that we can really measure radiation doses within the tissues, or even on the sur-

face; accordingly the only measurements which should be made in the radiological clinic relate to the characteristics of the radiation to be used. The knowledge derived from such measurements is insufficient for the proper correlation of cause and effect, but it is absolutely essential. In addition, the radiologist should utilize such data as are available to get an estimate of the dose which is effective in producing the observed results.

8. The principal characteristics of the radiation used in a treatment are: (*a*) the "intensity" and (*b*) the quality. At the present time the consensus of opinion is that intensity measurements can best be made by means of ionization instruments. The use of such an instrument is essential because the spark gap and the milliammeter do not give a definite indication of the intensity factor of the radiation emitted by an X-ray tube.

9. The quality of the radiation supplied by an X-ray tube is not completely defined by specifying the voltage and the filter. Additional information as to the wave-form and phase relations in the high tension generator is necessary. Owing to uncertainties in spark gap measurements and serious difficulties in the determinations of the wave-form and phase relations, it is more practical to specify quality by stating the following factors: (*a*) The general character of the high tension apparatus, (*b*) the peak voltage, and how determined, (*c*) the filter, and (*d*) the effective wave length (or the absorption coefficient or the half-value layer), stating how it was determined.

10. The measuring instrument to be used routinely in the radiological clinic should have a large ionization chamber and should be provided with means for periodic calibration. It should be definitely understood that this instrument is intended only for measuring the X-ray output of the machine. When voltage or filter or both are varied in treatment work, the radiologist should make use of the ionization instrument with the idea of obtaining a rough approximation of the treatment time with the new factors. He should then determine the desired duration of the irradiation by empirical means.

11. An ionization instrument with suitable means for periodic calibration, permits the radiologist to duplicate from day to day in his own clinic the essential treatment factors. But he cannot compare his treatments with those given in other clinics unless all instruments are calibrated in terms of the same unit. The *definition* of an International Unit of X-radiation was adopted recently at the Second International Congress of Radiology. In view of certain technical difficulties in the experimental definition of this unit, no standard instrument was adopted. For the present, therefore, there is no internationally recognized standard of comparison for the calibration of ionization instruments.

12. The United States Bureau of Standards is working on this problem and it will not be long before a *national* standard will be set up there. Then it will be possible to have instruments calibrated in terms of r-units, with the necessary degree of uniformity. It should be remembered, however, that instruments cannot be calibrated in r-units unless they meet certain minimum requirements.

13. In conclusion, the writer wishes to urge the radiologist to analyze the problem of radiation therapy into its component parts: clinical, pathological, and bio-physical. The purely physical aspects, while very important, do not play a preponderant part. This is evident when we consider that we are chiefly concerned with biological effects of radiation and that *purely physical* experiments can tell us nothing about such effects. On the other hand, biological effects and clinical results cannot possibly be

interpreted properly without a certain knowledge of the physics of radiation treatments. This knowledge should be sufficiently thorough to enable the radiologist to know the significance of physical measurements made in his clinic and to utilize intelligently data which have been obtained in the research laboratory.

THE SKIN ERYTHEMA FOR COMBINATIONS OF GAMMA AND ROENTGEN RAYS[1]

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THE reaction of the skin is a very important factor in external radiation therapy, since, in general, it limits the dose that can be administered. Consequently, any scheme which made possible the use of a larger amount of effective radiation without injury to the skin, would be of value. Recently some clinical evidence has been brought forward to show that when treatment is given by means of a combination of gamma and roentgen rays, the skin reaction is less marked than when only one type of radiation is used.

It seems worth while to investigate this matter, to see whether this is really the case, or whether the idea is based on erroneous determinations of the magnitudes of the radium and roentgen-ray doses administered. If it is found to be true, there remains the further problem of whether this combined treatment is more effective from the point of view of tumor regression. That depends on the possible selective response of the tissues to the radiations employed, and is entirely outside the scope of the present study.

The method of measuring the radiation administered is of primary importance. No physical means would be satisfactory, since it has not yet been shown that skin reaction is proportional to ionization or to any other physical phenomenon, over the range of radiations to be considered. The best, and simplest, way is to measure the radiation by the phenomenon being studied, the skin erythema. This makes unnecessary the use of any measuring instrument except to check the constancy of the roentgen-ray output. In our case it was found that under the same conditions (voltage, milliamperage, etc.), the roentgen-ray machine emits the same quantity of radiation from day to day, within very narrow limits. The radium, of course, will not change during the time of the research.

A method for investigating the effect of combining two types of radiation by this means has been used by one of us (E. H. Q.) in a study of the erythema dose for a combination of beta and gamma rays (1). It consists in, first, determining the separate erythema doses for the given types of radiation, and then in making tests of the skin reaction with combinations of the two. If 50 per cent of the erythema dose for one type, followed immediately by 50 per cent of the dose for the other, produces the same effect as 100 per cent of either one alone, then the combined dose, according to our standard, is the same as either single one. But if it takes, say, 60 per cent of each to produce the same reaction as 100 per cent of either, then the combined dose is less; there is an increase in the total amount that must be administered to produce the effect. In other words, the skin will stand more radiation if it is combined in this manner. As we have already stated, this gives no information about the therapeutic effects of the combination.

The inaccuracy of the skin erythema as a standard for measuring radiation has frequently been discussed (2, 3). The primary objection is the difficulty of determining the degree of reddening, or bronzing. We avoid this uncertainty by using the "threshold erythema," which has been discussed in our previous publications (4, 5). Briefly, it consists in determining the dose which, in 80 per cent of all cases, produces a visible

[1]Read by Mrs. Edith H. Quimby before the Radiological Society of North America at the Fourteenth Annual Meeting, at Chicago, Dec. 3–7, 1928.

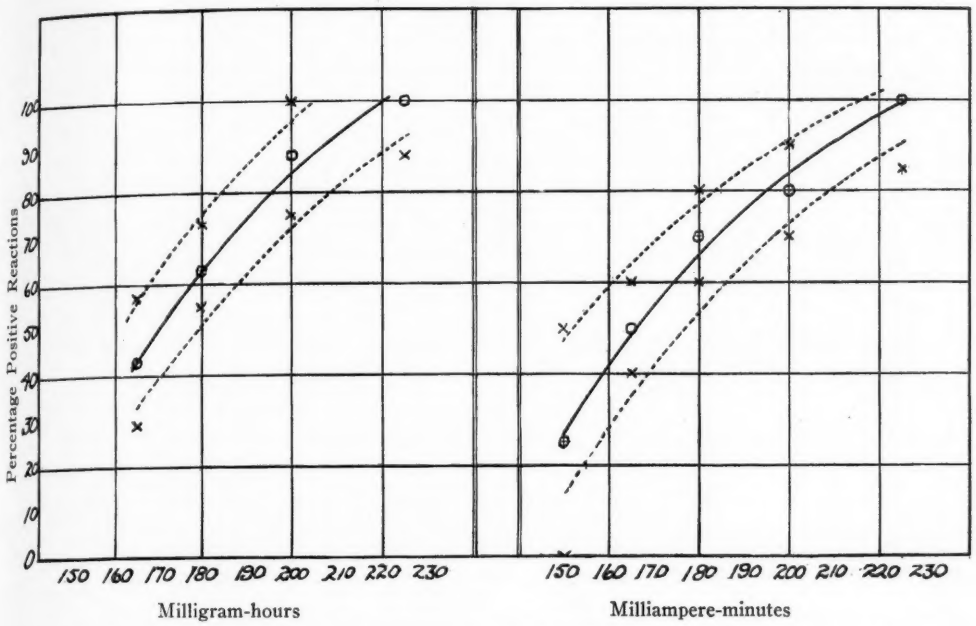

Fig. 1. Determination of threshold erythema dose for gamma and roentgen rays separately.

reddening or bronzing about two weeks after the treatment, and in the other 20 per cent produces no observable effect. While it is difficult to determine the degree of a reaction, it is simple to decide whether one is visible or not.

In the present investigation we studied the effect of combining gamma rays and roentgen rays of essentially the type used in deep therapy. The gamma rays were obtained from two platinum tubes containing 50 mg. of radium each. These were 0.5 mm. in wall thickness, 20 mm. long, 4 mm. in diameter, and were held side by side at a distance of 1 cm. from the skin in a container made of balsa wood and hard rubber. This container acted as a filter for secondary rays from the platinum. The roentgen rays were generated by a constant potential machine (kenotrons and condensers) operated at 165 K.V. (measured spectrographically[2]) and 3 ma., with a filter of 0.4 mm. of copper and 1 mm. of aluminum, a target-skin distance of 50 cm., and an area 3 by 3 cm. on the skin.

The threshold erythema dose for each of these types of radiation was first determined in the usual way. Table I shows the number of tests completed and the percentage of positive reactions in each set. This represents a total of 72 tests completed; 96 were made, but the remaining 12 patients (2 tests to a patient) left the hospital before the expiration of the two weeks' observation time, and did not keep their return appointments. The circles in Figure 1 represent these percentages, and the solid lines are the best smooth curves that can be drawn through them. On these curves, the point for 80 per cent positive reactions comes at 195 mg.-hr. for the radium and 195 ma.-min. for the roentgen rays. (The fact that both are 195 is merely a coincidence.) These, then, are the threshold erythema doses for our two types of radiation.

[2]The spectrographic method always gives lower voltage measurements than the spark gap. On a mechanical rectifier machine 165 K.V. according to the spectrograph is equivalent to about 200 K.V. measured by a 12.5 cm. sphere gap.

TABLE I

Dose	Radium		
Mg.-hr.	Number of Tests	Number Positive	Percentage Positive
165	7	3	43
180	11	7	63
200	8	7	88
225	8	8	100
	Roentgen Rays		
Ma.-min.			
150	4	1	25
165	10	5	50
180	10	7	70
200	10	8	80
225	6	6	100

We should like to consider here the experimental error of these dosage determinations. There is no error in the observations; a reaction is, or is not, visible. But since this is a borderline effect, we might easily have had in each group one or two patients of slightly different susceptibilities, who might have had different reactions. This probably would not happen in many cases; if the results actually obtained were not fairly accurate we would not find them so well represented by smooth curves of the correct general trend. If we investigate what would have happened in each set if one of the positive reactions for each dose had been negative, or *vice versa,* we should have a good idea of the possible error in the result. It is reasonable to believe that this range will cover the probabilities of the different results that might have been obtained with different sets of patients. The crosses in Figure 1 indicate the percentages of positive reactions for these assumptions; the upper ones are what we should have if one of the negative results in each case had been positive, and the lower if one of the positives had been negative. Any point falling within the band enclosed by the dotted lines would then be within the limits of experimental error. For 80 per cent positive reactions, on this basis, the radium dose is between 184 and 208 mg.-hr., and the roentgen-ray dose between 184 and 208 ma.-min. These doses might be expressed as 196 ± 12 mg.-hr. or ma.-min. This indicates that the experimental error may be about 6 per cent plus or minus.

For the effect of combined doses the procedure was as follows: The radium container was strapped to the patient's right leg, just above the knee (this being the area used in all the tests), and from 40 to 70 per cent of an erythema dose given. The area treated was outlined with ink and the

patient taken immediately to the roentgen-ray department, where he was given the corresponding dose of roentgen rays over the same area. A different dose of roentgen rays was given to the corresponding area of the other leg, and the patient returned to the ward for the proper dose of gamma rays to the second area. Thus two complete series of tests were made, in one of which the radium was applied first, in the other the roentgen rays. In very few cases did more than 15 minutes elapse between the successive radiations to the same area, and usually the interval was less.

In all, 100 tests were given with combined radiations, but complete observations were possible in only 79, with the results shown in Table II. In each case the dose administered was half gamma and half roentgen rays. There is no conclusive evidence that it made a difference which was used first. A curve plotted for the total percentages of positive reactions is shown in the solid line in Figure 2. From this it is evident that it takes a combined dose of 133 per cent to produce the threshold erythema, that is, 80 per cent positive results.

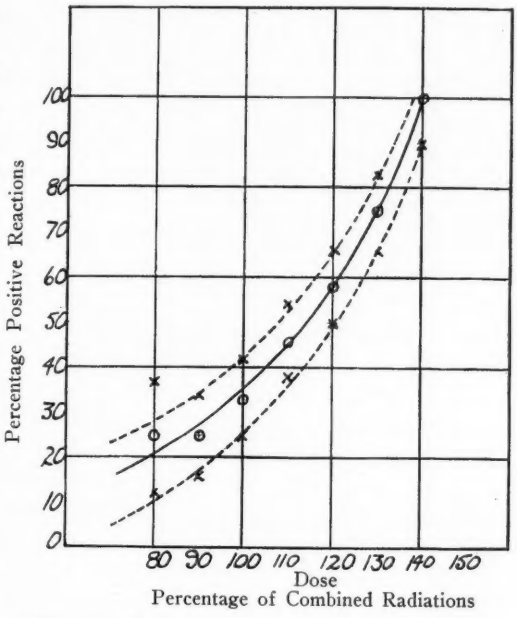

Fig. 2. Determination of threshold erythema dose for combined radiations.

The variation we would have had in this result if we had had a few patients responding differently to the tests may be investigated in the same manner as for the doses with the separate radiations. In each group, suppose one of the positive reactions had

TABLE II

Total radiation in terms of erythema dose Percentage	Number of Tests		Positive Reaction		
	Roentgen ray first	Radium first	Roentgen ray first	Radium first	Percentage total
80	5	3	1	1	25
90	5	7	2	1	25
100	6	6	2	2	33
110	8	5	4	2	46
120	7	5	3	4	58
130	5	7	3	6	75
140	5	5	5	5	100

been negative, or one of the negatives positive. The dotted curves in Figure 2 represent these cases, in the same manner as in Figure 1. The range within which 80 per cent positive results might be expected is then from 129 to 137 per cent for the combined radiation.

From these curves and tables it is evident that, for these two radiations *administered as stated above,* it takes a larger amount of the two in combination than of either one alone to produce an erythema.

This conclusion is not based on possible errors in determining the erythema doses. The error in determining the threshold doses has been shown to be probably not greater than 6 per cent plus or minus. If both the gamma and roentgen-ray doses used were 6 per cent too small, the combined dose which should give the threshold effect would be 112 per cent instead of 100 per cent. From the curves the lowest dose which could do it is 129 per cent, and the more probable one is 133 per cent. Even the lowest of these is well outside the margin of experimental error.

It is not easy to see why combining the two radiations produces such an effect. One fact that immediately suggests itself is that the distribution of the radiation in the skin and subcutaneous tissues is quite different in the two cases. Consequently, although the surface amount used is the same, the quantity of radiation arriving at any particular point may be greater or less in the combined treatment than in either of the single ones. Table III shows the percentages reaching different depths in the first centimeter of tissue, for the two types of rays used and for the "radium element pack" at a 6 cm. distance, as used in therapy. This last is included for the sake of subsequent discussion. Presumably anything deeper than 1 cm. will not influence a skin reaction. These measurements were made in the usual way, with a water phantom and small ionization chamber. In the case of the radium used in the skin tests, where the distance from the radium to the center of the chamber is only 1 cm., the results are probably not very accurate,[3] but they are at least suggestive.

TABLE III

Depth mm.	Percentage of Radiation		
	Roentgen rays	Gamma rays	Pack
0	100	100	100
2	99	77	95
5	97	53	86
10	93	29	76

By increasing the distance of the gamma-ray applicator the distribution could be made more uniform, but in order for it to be the same as for the roentgen rays, the distance would have to be in the neighborhood of 20 centimeters. Even to make the gamma-ray distribution similar to that of the pack as used in therapy would necessitate a distance of more than 6 centimeters. This would mean that with the same quantity of radium it would take two days to produce an erythema, and that in order to produce one in a time at all comparable with the roentgen-ray time, a much greater amount of radium would have to be used. Neither of these methods of application seems practicable from the experimental point of view, or expedient for the welfare of the patient used in the test.

It would be possible, by using a low voltage, short distance, and no filter, to obtain roentgen rays which would have the same distribution as the gamma rays. By using a combination of these roentgen rays and gamma rays, one could find out whether the

[3] Due to the relatively large size of the chamber in comparison to the distances used.

increase in tolerance to the combined radiations is due to the change in distribution or to some other action. If practically the same effect is found as in the present case, then the evidence is in favor of the increased tolerance being real, and not due to the change in the quantity of radiation received at different points. It would then be necessary to seek some other, probably biological, explanation.

In practice, however, we would probably never use two types of radiation having the same distribution. In the present work the softer one has been more evenly distributed in the tissues, due to its greater distance of application. By using a combination of two types of roentgen rays, one with high voltage, heavy filtration, and long distance, and the other with low voltage, light filtration, and short distance, we could reverse the situation and have the harder radiation more evenly distributed. Tests carried out under these conditions will give further information as to the effect of distribution of radiation in the tissues on the skin reaction. We hope to go on with these investigations in the near future.

In this connection we may call attention to the results obtained in the work already referred to, on a combination of two types of radiations, one predominantly beta, the other gamma. These experiments showed, when the radium was at the same distance from the skin for both types of radiation, greater tolerance for the combination than for either one alone. In this case the difference in distribution was also marked. It could, however, be overcome by increasing the distance for the soft radiation and decreasing it for the hard. An adjustment was found where both types had much more nearly the same distribution. Table IV shows the two sets of conditions. Tests carried out under the second showed the same increase in tolerance as under the first. In this case, then, the effect is not due to the difference in distribution of radiation in the tissues. Although under the second conditions the two radiations do not behave in identically the same fashion, they are close

TABLE IV

Depth mm.	Percentage of Radiation			
	Set 1		Set 2	
	Soft rays at 10 mm.	Hard rays at 10 mm.	Soft rays at 40 mm.	Hard rays at 5 mm.
0	100	100	100	100
1	62	82	70	75
2	39	69	51	57
3	27	57	39	46
5	14	42	25	30
7	8	31	19	19
10	6	24	14	14

enough, and different enough from the first set, to warrant this conclusion.

So far, we have used in our investigations only combined doses which were half of one type of radiation and half of another. It will be of interest to use other combinations, such as three-quarters of one and one-quarter of the other. It will be valuable to find out whether the greatest tolerance occurs when the dose is evenly divided between the two radiations, or for some other combination. Another point to be considered is whether one-quarter of one type of rays and three-quarters of another produce the same effect as three-quarters of the first and one-quarter of the second. These questions should be studied not only for the present combination of gamma and roentgen rays, but also for the other combinations of hard and soft roentgen rays, and of equally distributed gamma and roentgen rays already mentioned. This is a long program, but it will be necessary to carry out some such investigation before we can say whether this apparent increase in tolerance is due to changes in the amounts of radiation arriving at various points, or to an actual difference in response to the different types of rays, or to some other factor.

It is evident, therefore, that the work here presented must be regarded as preliminary. We have shown that it is true that, for particular applications of gamma and roentgen rays, the skin will tolerate more of the two types in combination than of either one alone. This does not justify the conclusion that, as the rays are employed in therapy, a larger amount can be administered if a combination is used. It does, however, lend support to the clinical evidence pointing in the same direction. It has no bearing whatever on the therapeutic efficacy of combining different types of radiation.

The authors wish to acknowledge their indebtedness to Dr. Failla, who first outlined this method. They wish also to express their thanks to members of the attending staff of Memorial Hospital, for their kind co-operation in supplying patients for these tests.

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RADIOSENSITIVITY[1]

By JAMES EWING, M.D., Pathologist to Memorial Hospital, NEW YORK

THE general laws governing radiosensitivity were recognized many years ago and have always been an important guide in radiotherapy. The early investigators soon observed wide differences in the reactions of various tumors and adjusted their methods accordingly. By 1915 it was possible to classify most of the well known tumors according to their sensitivity, giving the following general order:

(1) Lymphoma.
(2) Embryonal tumors.
(3) Cellular anaplastic tumors.
(4) Basal-cell carcinoma.
(5) Adenocarcinoma and adenoma.
(6) Desmoplastic tumors, such as squamous carcinomas, fibrocarcinomas.
(7) Fibroblastic sarcoma; osteosarcoma; neurosarcoma.

The law of Bergonie and Tribondeau was found to have a very uniform application and stated that tumors composed of rapidly multiplying cells, especially those of embryonal type and particularly those of the lymphoid group, are highly susceptible to radiation, and in such ratio as the above characters are developed.

In recent years it has become evident that the study of radiosensitivity may be carried very much farther than at first seemed possible; that there are important variations in this property in the subgroups of the major forms of cancer; that the factors entering into radiosensitivity are very numerous and sometimes rather obscure; that the general condition of the patient has important influence on the behavior of the tumor under treatment; that there is a definite relation, not always uniform, between grade of malignancy and radiosensitivity, and that all these matters require careful evaluation before radiation therapy can be intelligently conducted, and its results predicted. Thus a new field of investigation has been opened up, and now occupies the attention of investigators, both laboratory and clinical.

THE CAUSES OF RADIOSENSITIVITY

High metabolism of the tumor cells was early recognized as a prominent factor in radiosensitivity. It is so nearly synonymous with rapid growth that one may usually judge of radiosensitivity by rate of growth. Increased or unstable vascularity also goes with rapid growth, so that three factors are generally combined to render rapidly growing tumors sensitive to radiation. Indeed, hypersensitivity may be encountered in this class of growths, especially when they are bulky, and much caution must be used in their treatment in order to avoid accidents, such as interstitial hemorrhage and bulky necrosis. The vulnerability of mitotic nuclei and the abundance of autolytic cell ferments are probable factors of much importance in the sensitivity of rapidly growing tumors.

The embryonal character of the cells of origin renders the entire group of embryonal tumors highly radiosensitive. Their response to treatment is probably more rapid and complete than with any other group, so that radiologists have come to recognize these tumors as especially favorable. They are more sensitive than anaplastic tumors of equally cellular character. The grounds for this property are not entirely clear, but it seems to depend on the lability of the embryonal cell cytoplasm, delicate vascular supply, and the absence of any tendency to produce fibrous tissue. The essential malignancy of embryonal tumors is often overes-

[1]Read before the Radiological Society of North America, at the Fourteenth Annual Meeting, at Chicago, Dec. 3–7, 1928.

timated so that the favorable course may be due to absence of metastases, while the sensitive tumor is being destroyed.

The general physiology of the cells of origin largely determines the reaction to radiation. From this standpoint one may classify tumors according to their degree of sensitivity without regard to other factors, such as anaplasia or embryonal quality. At one extreme stand the lymphoid tumors, which, on account of rapid multiplication of cells, loose structure, and active metabolism, are among the most sensitive of all tumors. The adenocarcinomas and adenomas of glandular origin long tend to produce orderly glandular structures that resist radiation. Most of these glandular tumors tend to cause the growth of fibrous tissue which reduces their sensitivity. The presence of much mucus interferes with tissue reactions and reduces sensitivity. Epidermoid carcinomas arise from squamous cells which produce keratin and horny material, and these cells are highly resistant. Finally, there is a group of sarcomas of osteogenic or neurogenic origin, all of which yield much intercellular material which resists radiation. Throughout the entire list of malignant and benign tumors one can trace the influence of the intrinsic properties of the cells of origin.

Probably the most important factor which renders tumors resistant is the desmoplastic property or tendency to produce growth of connective tissue. This fact is observed most clearly with epidermoid carcinomas and various sarcomas, and with most glandular carcinomas, while it is absent with lymphomas and most embryonal growths. Even the most cellular anaplastic types of squamous epidermoid carcinomas and of sarcomas retain enough of this primitive function to render their complete sterilization difficult.

Opinions differ in regard to the influence of high vascularity on the behavior of tumors under radiation, but most observers attribute great importance to this factor. Highly vascular tumors melt down rapidly under radiation from necrosis of capillary endothelium, often with interstitial hemorrhage and sometimes with dangerous intoxication. Or the slow progress of obliterating endarteritis may sooner or later shut off the blood supply and lead to bulky necrosis and late sloughing. Wherever bulky necrosis occurs in a tumor I am strongly inclined to refer the change to obstruction of blood vessels, and under many other circumstances the necrosis of tumor cells appears referable to occlusion of vessels by a variety of methods.

The location or bed of the tumor has much influence on the results of radiation. Everyone is familiar with the resistance of tumors growing in bone. In fat tissue tumor cells find abundant sources of nourishment, but are protected from a ready attack by leukocytes and granulation tissue. Much of the difficulty of treating mammary cancer is probably due to growth in the fat tissue of breast and axilla. Moreover, in such tissue the capsules of lymph nodes are poorly developed and readily traversed by tumor cells. Tissues altered by previous inflammation, especially by syphilis, are readily invaded by tumor cells, but give poor conditions for the curative reactions from radiation. One the other hand, the lymph nodes enjoy peculiar advantages from the control of tumor cells. The distended capsules restrict the circulation and exert pressure on the growth. Lymphocytes and plasma cells have a controlling and even destructive effect on many tumor cells. Under some circumstances lymph nodes produce much cellular granulation and connective tissue, which incarcerates and destroys tumor cells.

Many have observed that active infection interferes with successful radiation, but it is difficult to trace the exact reasons. Treat-

ment generally aggravates the inflammatory process, sometimes seriously. In the edematous softened tissue the tumor cells sometimes seem to grow with increased activity. In cervical cancer I have seen very numerous mitoses about minute foci of polynuclear leukocytes, causing pain, sloughing, and hemorrhage. On the other hand, a great abundance of polynuclear leukocytes must be assumed to be inimical to the growth of tumor cells, but as a rule the active exudation of these cells seems to prevent the appearance of lymphocytes, plasma cells, and granulation tissue, which are more effective in destroying tumor cells.

The general condition of the patient determines the results of radiation, regardless of nearly all other factors. In fresh subjects in good general health, without anemia or cachexia, the results of radiation are usually prompt and definite, whereas in anemic and cachectic subjects with poor circulation, tumors may fail entirely to respond. In such anemic subjects, little advantage is gained by treatment, and often the condition of the patient is made worse, while the tumor is unaffected. Blood transfusions are, therefore, of much advantage in many circumstances. Such observations form the basis of the belief that active circulation in the tumor is essential to radiosensitivity, that the body reacts as a whole organism, and that a constitutional element plays a part in any favorable response to treatment. Stated in other words, high general vitality of tumor and host are essential factors in radiosensitivity, so that a sound clinical point of view must govern radiation therapy.

A most important and remarkable phenomenon is the acquired resistance to radiation following successive inadequate dosage. After several treatments, usually when they have been of considerable severity, tumor cells may become radium-fast and fail to yield even to very high dosage. That they have not, at the same time, lost vitality is shown by the occasional flares from such indolent tumor foci, which may spread with marked rapidity, giving the impression that the tumor has been stimulated and its growth capacities increased. In nearly all such cases one finds that the persistent tumor cells lie in dense hyaline avascular fibrous tissue, where they are protected from the attack by leukocytes and blood serum. This condition may be called "abortive fibrosis." It forms a strong argument in favor of the view that the destruction of tumor cells by radiation results largely from a normal inflammatory tissue reaction.

RELATION OF RADIOSENSITIVITY TO MALIGNANCY

In general, the degree of radiosensitivity runs parallel to the degree of anaplasia of tumor cells, but so many factors enter into clinical malignancy that the parallel is far from uniform. In the group of glandular tumors one may recognize several grades of malignancy—adenoma, adenoma malignum, adenocarcinoma, alveolar carcinoma, and diffuse carcinoma—and here the sensitivity increases in the order named. Among epidermoid carcinomas, the adult squamous tumors are resistant, basal-cell varieties are more sensitive, while transitional-cell carcinomas and lympho-epitheliomas are highly sensitive. The fact that highly cellular malignant tumors, which give bad results with surgery, are markedly radiosensitive suggests that these tumors should be treated by radiation in preference to operation, and this plan is now being followed in many clinics.

Exceptions to the rule that cellular tumors are sensitive are not infrequent. Melanoma is generally both cellular and resistant. Giant-cell tumors of bone are benign but highly sensitive. Embryonal adenomas and carcinomas are generally less malignant than their structure indicates, but nearly always

very sensitive. A distinction may be made between primary sensitivity and curability. Many cellular tumors of all classes melt down under radiation, but do not disappear completely and recurrences develop from the remnants. The physiology of the cell of origin may determine the results. Thus many carcinomas yield scar tissue inclosing resistant foci of tumor cells. Endothelioma of bone may fail to be completely resolved because the final product is fibrous and persistent tumor cells are protected from complete solution. On the other hand, lymphosarcoma has no tendency to produce fibrous tissue, and resolves completely. Hodgkin's granuloma produces much connective tissue and is difficult to resolve completely.

As a result of the many new observations on degrees of malignancy and radiosensitivity, tumor diagnosis has become much more complex and difficult and at the same time more serviceable. Among the fruits of this study has been the recognition of several new varieties of tumors. Thus Regaud and Schmincke, in 1921, finding some epidermoid carcinomas of the nasopharynx highly radiosensitive, traced the cause to the peculiar physiology of the cells of origin, and established the group of lympho-epithelioma. In the same way the peculiar sensitivity of a common tumor of bone forced the conclusion that its histogenesis was peculiar, and thus endothelial myeloma came to be recognized. Among the common forms of glandular carcinomas of breast, uterus, mucous membranes, stomach, adrenal, kidney and other organs, the observed differences in malignancy and radiosensitivity are so great that the estimation of these differences becomes an urgent and difficult task for the pathologist, and an important guide for the therapeutist. No one may safely engage in radiotherapeutics unless he is prepared to take due cognizance of these factors. The extremely cellular anaplastic forms of rectal and cervical cancer give a very bad prognosis from surgical removal, but their radiosensitivity is so great that a high proportion of cures is obtained from radiation, and we thus have the paradoxical situation that the more malignant the tumor, the better is the prognosis. Among the epidermoid carcinomas there are so many differences in structure, radiosensitivity, and clinical malignancy as to require the separation of these tumors into well defined subgroups. At the Radiological Congress in Stockholm, in July, 1928, I ventured to offer the following classification of epidermoid carcinoma, based upon probable histogenesis and observed radiosensitivity:

(1) Squamous carcinoma, malignancy of varying grades, *radioresistant.*

(2) Transitional-cell carcinoma, malignancy high, *radiosensitive.*

(3) Schneiderian carcinoma, malignancy high (subvariety of transitional-cell carcinoma), *radiosensitive.*

(4) Basal-cell and adenoid cystic carcinoma, malignancy low, *radiosensitive.*

(5) Lympho-epithelioma, malignancy high, *very radiosensitive.*

Throughout the entire group markedly anaplastic cases show increasing malignancy and radiosensitivity.

Among the glandular carcinomas similar subdivisions may be established, in which the variations in clinical malignancy and sensitivity are so great as to render the cases different practical problems.

Among the sarcomas, osteogenic, neurogenic, and even lymphosarcoma, the cases vary greatly in degree of anaplasia and sensitivity, and these variations are found to determine largely the clinical course and the results of treatment.

It is obvious that in a field so broad and complex as the structure of tumors many years of observation will be necessary before our knowledge permits the accurate estimation of the degrees of malignancy and radio-

sensitivity. In this task no fixed rules can apply, and only experience counts. It is clear, however, that the pathologist who undertakes the diagnosis of tumors can no longer discharge his function by reporting simply "carcinoma" or "sarcoma," nor even with the far more significant diagnosis of the tissue of origin, where this is possible, but is required to acquaint himself and the clinician with the grade of malignancy and the degree of radiosensitivity. In order to accomplish this difficult task, he must apply himself cordially to this new and interesting inquiry into the physiological and clinical phases of tumor growth.

To the radiotherapeutist a knowledge of the grades of malignancy and radiosensitivity is of the first importance. It enables him to form a more accurate impression of the actual condition of his patient, and the natural course of the disease. He will be able to anticipate lymphatic and distant metastases, or to set aside these developments as improbable. Knowing what radiation can or cannot accomplish, he will have a sound basis for planning treatment, both as to in-

DETERMINATION OF RADIOSENSITIVITY

Embryonal quality	Slight + 20	Marked + 40	Pronounced + 50
Anaplasia	Slight + 10	Marked + 15	Pronounced + 20
Lymphoma	Simple + 10	Reticulum cell sarcoma + 15	Atypical + 20
Epidermoid carcinoma	Adult — 10	Transitional basal cell —0	Lympho-epithelioma + 20
Glandular carcinoma	Adenoma — 10	Adenocarcinoma — 5	Carcinoma — 0
Desmoplastic quality	Slight — 10	Marked — 15	Pronounced — 20
Neurogenic sarcoma	Fibro- — 30	Cellular — 0	Atypical + 10
Osteogenic sarcoma	Bone formers — 30	Periosteal fibrosarcoma — 5	Cellular vascular types — 0
Bed of tumor	Bone scar — 40	Normal 0	Lymph nodes + 5
Condition of patient	Normal 0	Anemic — 10	Cachectic — 40

tensity of dosage and scope of the field to be irradiated. He will not attempt to destroy squamous carcinoma or neurogenic sarcoma with half-erythema doses of external radiation, nor will he insert radium seeds into lymphosarcoma or lympho-epithelioma.

In the therapeutic test by radiation, he will find a method of much value in determining the presence or absence of tumor tissue, and its probable nature, without biopsy.

When due progress has been accomplished along these many lines of study which now lie open in the finer diagnosis of tumors, and when this knowledge is intelligently employed in laboratory and clinic, then the treatment of tumors, both by surgery and radiation, will be relieved of much of its present haphazard empiricism, and the outlook for the cancer patient will be vastly improved.

The accompanying table presents a scheme of the factors entering into radiosensitivity and offers a provisional estimate of their importance. The table is sophistical in so far as it may suggest that the degree of sensitivity may be calculated with mathematical accuracy, but it suggests the method by which one may arrive at an approximate estimate.

It is obvious that single factors in any given case may outweigh all others, and that the true estimate can be reached only by experience and long observation of cases.

THE RESPONSE OF VARIOUS TYPES OF BREAST CANCER TO RADIATION[1]

By FRANK E. ADAIR, M.D., Attending Surgeon, Memorial Hospital, NEW YORK

CANCER of the breast, when compared with cancer in other regions of the body, is fairly radioresistant. One constantly sees those cases in which radiation of various types has been totally ineffective in either slowing-up the progress of the disease or in preventing metastasis. In fact, the majority of breast carcinomata belong to this group.

On the other hand, we occasionally encounter cases in which irradiation of even a very mild degree, as well as that of heavy intensity, has caused profound tissue changes, resulting in diminution of the tumor bulk or causing its complete clinical disappearance. It is the study of this latter group that encourages and impels us to press radiation further. It gives us a hope that we will eventually attain an exact radiation technic which will afford us a thoroughly reliable and effective therapeutic agent.

The intrinsic attributes of the individual tumor to be treated are of equal, if not more, importance than the type of irradiation employed. Many of the individual characteristics of the tumor cannot be estimated clinically. Experience in and study of the various types of breast cancer give us a clue as to the result to be anticipated by irradiation of that tumor. We should by this time be familiar with the effect of radiation upon bulky adenocarcinoma, on Paget's disease, on inflammatory carcinoma, on scirrhous carcinoma, and cystadenocarcinoma. In this first group of five types it is possible to make a clinical diagnosis because each has its own outstanding characteristics. Having made the exact anatomical diagnosis, it is, therefore, possible to prognosticate as to the radiation effect on these five types.

There is a second large group of cases in which it is not clinically possible to know the exact pathologic anatomy. However, in one's attempt to diagnosticate the type of tumor, he is materially assisted by the use of radiation as a diagnostic test. This is also called the "therapeutic test." If radiation be applied to the tumor as a test, and the tumor promptly diminishes or disappears, one may be quite certain that he is dealing with a highly cellular type, such as the medullary or the anaplastic. One does not obtain this diminution or disappearance in fibrocarcinoma or diffuse duct carcinoma.

The tissue changes resulting from irradiation have been carefully detailed by Ewing in the Carpenter lectures, so that we will largely confine ourselves to pointing out the types of breast cancer which are radiosensitive and those which are not. There is every gradation in these tumors, between the extremely radiosensitive and the highly resistant. On the other hand, one must not take away the impression that radiosensitivity runs parallel to longevity.

Unfortunately, marked radiosensitivity is no criterion of the ultimate ease of cure. As a matter of fact, the more radiosensitive a carcinoma, the more cellular; the more cellular, the more dangerous, and the more subject to distant metastases. Our desire and purpose is to obtain not only tumor-disappearance, but, what is even more important, tumor-restraint. Radiation accomplishes the latter by the locking-up processes of fibrosis, lymphocytic infiltration, and calcification. Surgery to-day, in our best clinics, is accomplishing from 35 to 38 per cent of five-year cures in breast cancer. The employment of radiation to date has not materially raised the percentage of five-year cures in the operable cases. The Memorial

[1]Read before the Radiological Society of North America, at the Fourteenth Annual Meeting, at Chicago, Dec. 3–7, 1928.

Hospital has a five-year cure record of 39½ per cent. This is by the combined use of a pre-operative radiation cycle, the employment of a radical mastectomy, followed in about six weeks by a post-operative radiation cycle.

Even though it would appear that the employment of radiation has improved our results, albeit to a small degree, we strongly feel at the Memorial Hospital that this work should be vigorously pushed. Eventually we will become familiar with the types in which its employment seems valuable.

Radiation in breast cancer, if for no other reason, is a valuable therapeutic agent for the relief of pain and the treatment of recurrences, but to draw sweeping conclusions as to its curative value would be premature. In general, those cases which are easily cured by surgical methods are also easily cured by radiation.

There is tremendous confusion in the medical mind on the subject of classifications of breast cancer. Each textbook gives a different classification. Descriptive terms are many times employed by pathologists which are not fully comprehended by the clinicians.

The histologic and the histogenic nomenclatures are easily mixed, and are confusing. However, there is an absolute necessity for the clinician to obtain a clear idea of some classification which will serve as his guide. The following classification will be used in this paper. It may not be adequate to cover all the more rare types, but it will be comprehensive enough to include the most important ones.

(*a*) Duct Carcinoma
1. Scirrhous
2. Medullary
3. Diffuse duct
4. Paget's disease
5. Inflammatory
6. Anaplastic

(*b*) Adenocarcinoma
1. Cystadenocarcinoma
2. Bulky adenocarcinoma
3. Sweat gland
4. Gelatinous
5. Anaplastic

(A) DUCT CARCINOMA

1. *Scirrhous.*—Scirrhous cancer gives a distinct clinical picture. It is the type in which there is the tremendous overgrowth of fibrous tissue, enmeshing a comparatively small number of carcinoma cells. The breast becomes shriveled and retracted against the chest wall. If this process continues, there will, many times, be complete disappearance of the mammary organ. The process is slow. This tumor occurs in the later periods of life, and, as a rule, the diagnosis is easily made. The employment of radiation over such a tumor has very little obvious effect. It may slow up the process somewhat, but it never causes its disappearance, and we should not consider scirrhous carcinoma as a radiosensitive type. Radiation is probably wise, but the disease progresses slowly in spite of it.

2. *Medullary.*—This is a type of duct carcinoma in which a clinical diagnosis cannot be determined. It has no distinct clinical picture. The history is sometimes of help because of rather rapid growth, but this feature must many times be discounted because in a large breast any history of rate of growth is unreliable. This cellular type is radiosensitive, and very frequently we see complete disappearance of palpable tumors. We feel that this type should be heavily radiated, not only in order to destroy the tumor cells but to produce fibrosis and lymphocytic infiltration, and thereby hold the tumor as a local process.

3. *Diffuse duct.*—This is an interesting clinical type, and easy of diagnosis. The picture presented is that of breast tissue

completely infiltrated, but having no distinct discrete hard tumor. There is edema of the entire breast, giving a marked "orange-peel appearance." The dependent portion of the breast has a typical "water-logged appearance." This tumor completely fills the mammary system of the breast involved; the ducts and acini are distended and filled with tumor cells. Radiation of the diffuse duct carcinoma is not very effective. On the other hand, radiation employed over the axillary metastasis shows that the metastasis is markedly radiosensitive.

4. *Paget's disease.*—Paget's disease of the nipple is a clinical entity, rather easy of diagnosis. Two pathologic processes are taking place simultaneously: there is the newgrowth of the nipple as well as a newgrowth in the terminal ducts behind the nipple. Ulceration of the nipple usually accompanies this disease. The nipple tumor in its earlier stages is radiosensitive, and we feel that the underlying breast tumor is also radiosensitive. We have one case which came three years ago with a typical ulceration of the nipple and marked thickening behind the nipple. A small section was made from the nipple, and the diagnosis of Paget's disease was confirmed. The patient received a radium tray of 3,000 millicurie-hours at a distance of 3 centimeters over the nipple. This was followed by one high voltage roentgen-ray treatment over the breast, and another over the axilla. There was prompt disappearance of all palpable disease, and the patient has remained free of disease as far as it is possible to tell. In general, I feel that nipple carcinoma is radiosensitive, as we have had complete disappearance and freedom from disease for a period of from two to three years in three instances of adenocarcinoma of the nipple.

5. *Inflammatory.*—This is one of the most striking clinical pictures in the entire realm of breast disease. Inflammatory carcinoma is characterized by a reddening of the skin over the part of the breast involved. There is a distinct ridge or elevation at the site, and a localized increase of temperature of from 2° to 3°. There is thickening and rather board-like hardness of the skin itself, due to the fact that all the lymphatic spaces in the derma are plugged with groups of carcinoma cells. It is an extremely cellular type of mammary carcinoma, and extremely lethal. Superficial radiation by roentgen rays over the site will cause complete regression of this tumor. However, most of the patients with this type of cancer die from distant metastases, particularly intra-abdominal.

6. *Anaplastic.*—This offers no distinct clinical picture. It is commonly mistaken for fibroadenoma or some other benign growth. It occurs principally in women under thirty-five. The surgeon removes this small tumor and is surprised to find that it is a cancer. This may be followed by a radical mastectomy. Rather promptly, one finds distant bone metastasis. It is a particularly discouraging type—extremely radiosensitive on account of the character of the cells, but the end-results are bad.

(B) ADENOCARCINOMA

We will now consider the various types of adenocarcinoma.

1. *Cystadenocarcinoma.*—This type has a distinct clinical picture and history. It is usually accompanied by a history of bleeding from the nipple. The growth originates in the terminal ducts behind the nipple or at the edge of the areola. It becomes rather bulky, and remains localized for a long period before metastasizing. It is not radiosensitive as a whole, though portions of it may be, but the major part of the growth is papillary in type.

2. *Bulky adenocarcinoma.*—This tumor is characterized by being a rather large growth which remains localized for a long period before metastasizing to the axilla or invading the remainder of the breast. It in-

volves the skin, breaks down, and becomes a necrotic foul-smelling mass. It appears to be a worse type than many of the others which are in reality far more lethal. Radiation should be sparingly administered, as this is not a radiosensitive type, and heavy radiation over it easily causes a breaking-down of the tumor.

3. *Sweat gland.*—The sweat gland carcinoma, when located at the fold of the breast and the chest wall, is usually easy of diagnosis. It remains for quite a period as a strictly localized tumor process, not involving the skin. There is skin attachment but no true dermal invasion. When the sweat gland carcinomata appear in the breast substance, then it is not clinically possible to accurately diagnose the type. Sweat gland carcinoma is radioresistant. We have no instances of complete disappearance of this tumor under radiation.

4. *Gelatinous.*—This is a very rare form of breast cancer. Some clinicians feel that it is possible to make an accurate diagnosis of the type, but we have not had a sufficient number of cases to enable us to formulate a clinical picture that is dependable. We can say nothing as to the radiosensitivity of this tumor.

5. *Anaplastic.*—The clinical picture here presented, so far as our experience goes, is the same as that described under the heading of "Anaplastic Duct Carcinoma."

We would like to state here that treatment of recurrences seems most effective when the recurrence is superficial and thoroughly accessible to radiation. One of the most impressive types of recurrence, and one which offers a brilliant result from radiation treatment, is the rather bulky sternal metastasis. From such a recurrence, treated by a radium pack of 12,000 millicurie-hours at a distance of 6 cm., we have not only had complete regression and disappearance of the recurrence, but the patient has remained free of disease, in one instance for six years and in another for four years. It is very common to see complete disappearance of bulky axillary and supraclavicular metastases in the more cellular forms of carcinoma. However, these metastases recur with great frequency.

During the past year we have been much impressed by the treatment of chest metastasis in cases of extremely cellular tumors. Recently we have been so much pleased with the temporary clearing up of the dyspnea, and the general improvement, that we are going to more vigorously treat chest metastases.

VARIATION IN RADIOSENSITIVITY OF EPIDERMOID CARCINOMA OF THE CERVIX UTERI[1]

By WILLIAM P. HEALY, M.D., Attending Gynecologist, Memorial Hospital, NEW YORK

CARCINOMA of the uterine cervix was one of the first of the major forms of malignant disease to be systematically treated by radium and the roentgen ray. It offered a favorable field for trial of the method, not only because of the large number of cases available but because of the facility with which the lesion could be observed and the treatments repeated if necessary.

Since radiation therapy has come into vogue it has been increasingly evident that carcinoma of the cervix responds, on the whole, unusually well to this method of treatment.

It was observed, also, that under radiation therapy many cases apparently hopelessly involved in an advanced stage of cervical cancer improved to a much greater degree than other cases, clinically less advanced in the disease and seemingly more favorable for successful treatment. Various theories and explanations have been advanced to account for these results. In general, it has been assumed that the failure of cases that appeared to be clinically similar to respond alike to the same plan of treatment depended largely if not entirely upon the individual's own resistance or susceptibility to the disease.

A study of the histologic structure of the primary growth in the cases seen at the Memorial Hospital indicated that approximately 96 to 98 per cent were squamous epidermoid carcinomata arising from the mucous membrane of the portio vaginalis, and 2 to 4 per cent were adenocarcinomata arising from the cells of the cervical mucous glands.

For some years many writers have attempted to subdivide the large group of squamous epidermoid carcinomata into smaller groups, based upon variations in cellular, nuclear, and stromal characteristics. These subdivisions have now come to be well recognized by pathologists. Moreover, some investigators have assigned varying degrees of malignancy to these different groups, and, in general, have regarded the more fully developed adult squamous-cell tumor as being less malignant than the transitional cell or plexiform tumor, and the latter, in turn, as less malignant than the embryonal or anaplastic cell type of tumor.

Based upon this grouping it would seem as if the third, or anaplastic, cell tumor type, being the most highly malignant, should give the worst prognosis. Tumors of this group have been and still are regarded histologically and clinically as representing the potentially most malignant group. No doubt, if untreated, it would seem reasonable to assume that they would progress to a fatal termination more rapidly than the cases in Group 1 or 2.

Likewise, when treated along surgical lines, by complete hysterectomy, the five-year end-results have been extremely poor, as indicated by the reports of Martzloff from the Johns Hopkins Hospital and Broders from the Mayo Clinic. Each of these writers reports only 9½ per cent of five-year cures in this group.

Since the publication of Broders' classification of epidermoid cancers into four histologic groups we have been studying the histologic structure of all our biopsy specimens and dividing them into three major groups, based upon the degree of anaplasia

[1]Read before the Radiological Society of North America at the Fourteenth Annual Meeting, at Chicago, Dec. 3-7, 1928.

present in the cells and the relative amount of stroma present.

As a rule there is no great difficulty in deciding, after a study of these criteria, in which one of the three groups the case belongs. Occasionally, however, one does meet with a borderline case which might readily be placed in Group 1 plus or Group 2 minus. The final decision in such a case is based upon the histologic evidences against or in favor of radiosensitivity in the specimen.

The same plan is followed when in doubt between Group 2 and Group 3. It is evident, therefore, that the knowledge which has been acquired in recent years of the differences in behavior of different histologic structures in response to radiotherapy is of the utmost value in making this classification.

The question has been raised, especially by Martzloff, as to whether or not the biopsy specimen is a true index of the histologic structure of the parent tumor. We confess that there has been considerable doubt in our mind regarding the correct answer to this question. We have endeavored to check it up by multiple biopsies done on different days and have been greatly interested to find that the laboratory report on the grouping of the specimen seldom changes. From time to time the laboratory will decline to group a specimen because of insufficient tissue or because the neoplastic qualities are obscured by infection and inflammatory reaction.

On the whole, our experience with the study of biopsy specimens and grading or grouping of the cases as a result of this study has been sufficiently satisfactory and reliable to permit of its use as a routine method of real practical value.

The first intensive study of our cases on this basis was made by Dr. Max Cutler, who reviewed the slides of 200 cases treated in 1922 and 1923. His study seemed to indicate that classification of epidermoid carcinoma of the cervix into three histologic grades, based upon the degree of anaplasia present, was a practical one. Also, it seemed to indicate that these three groups corresponded to three degrees of potential malignancy: Group 1, low; Group 2, medium; Group 3, high malignancy. Moreover, there seemed to be a corresponding variation in the degree of radiosensitivity of the different groups.

Group 1, made up of cells adult in character, highly differentiated, with a tendency to hornification and the formation of pearls, was resistant to radiation.

Group 2 cases, the plexiform type in which the cells show moderate anaplasia, few or no squamous characters, partial loss of polarity, a plexiform arrangement of the cells, and moderate tendency to infiltration, are decidedly more radiosensitive than the cases in Group 1.

Group 3, in which there is an absence of squamous characters, comprises a diffuse infiltrative growth and complete loss of differentiation of cells. It is highly radiosensitive.

The percentage of cases in the different groups was: Groups 1 and 3, approximately 20 per cent each; Group 2, 60 per cent. It is thus seen that about four-fifths of the cases occur in Groups 2 and 3, which are or tend to be radiosensitive. This no doubt helps to explain the favorable results obtained by radiation therapy in carcinoma of the cervix. It also aids in offering a solution for the marked improvement observed in some quite advanced cases and the poor result obtained at times in apparently favorable cases. It is evident that the more anaplastic the cellular structure of a tumor, the more malignant it will be, and, likewise, the more radiosensitive and the more favorable for radiation therapy.

Thus a strange situation arises in which we find greater malignancy associated *pari*

passu with a more favorable prognosis, when radiation therapy is the method of treatment used in carcinoma of the cervix.

Of course, one must never lose sight of the fact that the earlier the diagnosis is made the more favorable the prognosis, regardless of the cell type or group.

TABLE I

EFFECT OF CLINICAL STAGE OF DISEASE UPON END-RESULTS

Clinical Stage	Per Cent Well Five Years
Early	60
Borderline	37
Advanced	23

CONCLUSION

It would seem, therefore, that a study of the histologic structure of epidermoid carcinoma of the cervix, combined with the knowledge of the radiosensitivity of the cellular structures concerned, offers a sound and satisfactory explanation for the favorable results of radiation therapy obtained in this field.

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TABLE II

EFFECT OF HISTOLOGIC STRUCTURE UPON END-RESULTS IN THE DIFFERENT CLINICAL GROUPS

		RADIATION		
Cell Type	Stage of Disease	Total No. Cases	No. Well	Per Cent Cured Five Years
Adult (Grade 1)	Early and Borderline	10	5	50
	Advanced	25	1	4
Plexiform (Grade 2)	Early and Borderline	21	9	43
	Advanced	102	15	14
Anaplastic (Grade 3)	Early and Borderline	9	6	66
	Advanced	33	14	42

CHANGES IN PRIMARY AND METASTATIC BONE TUMORS FOLLOWING VARIOUS DOSES OF ROENTGEN RAY[1]

By RALPH E. HERENDEEN, M.D., NEW YORK

THE response of primary bone tumors or the changes induced by the application of a known amount of roentgen or radium rays can be predicted with a fair degree of accuracy, provided certain other information is available. The additional knowledge is the same which is required by the radiologist, surgeon, or pathologist for estimation of the degree of malignancy and the sensitivity of other groups of tumors to roentgen or radium rays. In other words, it may be said that the response of primary bone tumors to irradiation is governed by the same general rules followed in selecting the amount of irradiation in the treatment of other groups of tumors.

That there are exceptions to these rules, and that the degree of reaction or response varies within wide limits, is well known, but if due consideration is given the following factors, the sensitivity of the tumor may be measured.

Of all the factors to be considered, none is of more importance than the age of the patient; but equally so, of course, is a detailed knowledge of the character of the tumor in a given case. By "character" is meant degree of malignancy, rate of growth, size, location, origin, and tendency to produce or destroy bone.

The clinical evidence of the response of bone tumors to irradiation is often delayed in the presence of certain chronic constitutional diseases, fractures, infection, or following incision for biopsy, and considerable care must be exercised in administering the larger doses which seem necessary to obtain the desired results, lest damage be done to normal tissue and consequent delay in bone regeneration result.

The question of the additional information obtained by submitting a section of the tumor to a pathologist is a subject by itself, but it seems that in other fields the biopsy as a routine procedure for the combined purpose of determining the diagnosis, degree of malignancy, and sensitivity of cells to irradiation is wholly justifiable. However, this method of obtaining information regarding bone tumors only occasionally supplies knowledge which may not be obtained through other procedures, while balanced against the knowledge obtained must be considered the hazards of dissemination of tumor cells and infection. Furthermore, the repair process following irradiation may not only be delayed, but the effect or indirect action of irradiation on the tumor cells may be reduced to a minimum.

If enumerated in order of sensitivity, primary bone tumors may be classified as follows:

(1) Endothelial myeloma or Ewing's tumor.
(2) Giant-cell tumor.
(3) Multiple myeloma.
(4) Osteogenic sarcoma of the destructive type.
(5) Osteogenic sarcoma of the mixed or destructive and productive type.
(6) Osteogenic sarcoma of the sclerosing bone-producing type.

When it comes to considering the sensitivity of metastatic or secondary bone tumors, the question of determining the effect of irradiation becomes less certain and more complex.

[1]Read before the Radiological Society of North America, at the Fourteenth Annual Meeting, at Chicago, Dec. 3–7, 1928.

Although it may be true that, in general, carcinomas require much larger doses than sarcomas, and that approximately 100 per cent should be administered to carcinomas as against 80 per cent to sarcomas, this should be regarded only roughly as a guide and of but little practical assistance in the treatment of individual cases.

As an example, it is doubtful if epidermoid carcinomas of the cervix in middle-aged patients are more resistant as far as clinical evidence is concerned than the sclerosing bone-producing osteogenic sarcomas in young adults.

It is probable that the greatest number of secondary bone tumors which the radiologist is called on to treat result from metastasis from mammary cancer. The histologic variety of these tumors, the wide range in age, the numerous locations in bones in which metastasis occurs all make for variations in response difficult if not almost impossible to anticipate. It may be said, however, that in general the response of these tumors as compared with the response of other carcinomatous metastasis to bones, as indicated by relief from pain and evidence of attempt at repair, is more prompt and indicates a sensitivity seldom demonstrated in carcinomatous metastasis from other glands.

Of all the destructive types of carcinomatous metastasis to bones, it appears that the hypernephroma is one of the most resistant to irradiation. The reason for this is not clear, for it occasionally appears that irradiation of the primary tumor is followed by prompt and definite diminution in size. The vascularity of these tumors is a prominent feature, and it is probable that the changes in the primary tumor are due largely to the effect of irradiation on the blood vessels.

Metastases to bone from carcinoma of the bladder are also comparatively resistant to radiation.

Fig. 1, Case 1. Early but extensive endothelial myeloma. Bulky soft-part tumor. Radiograph shows relatively little bone change, although the ulna is extensively involved.

In metastasis from carcinoma of the prostate a film of the pelvis frequently demonstrates an unusual but characteristic behavior on the part of the bone involved. Numerous diffuse dense sclerotic or osteoplastic areas are seen, and the only effect obtained from irradiation has been in some instances relief from aching and pain.

The response to irradiation in invasion of bone and metastasis from carcinoma of the cervix is, as a rule, disappointing as compared with the results in metastasis from the breast, and the same may be said

Fig. 2, Case 2. Showing character of bone changes. Section of tumor reported by Ewing. Endotheliomyeloma.

Fig. 3, Case 3. Showing resemblance to Case 2. Endotheliomyeloma before roentgen-ray therapy.

regarding carcinoma of the mouth, tongue, and lip.

The majority of cases of endothelial myeloma or Ewing's tumor occur in children. These tumors are characterized by rapid growth; there is an increase in local heat; the patient frequently runs a temperature of 100° or 102° F. These findings, along with the film of the part, lead to a diagnosis of osteomyelitis more frequently than to that of Ewing's tumor. The X-ray film, in order to be of value, must be an excellent one, and several exposures at different angles should be obtained. At first glance they may appear negative, and films of the opposite or corresponding bone may be necessary to show the faint changes which take place in an early case. The tumor may be quite bulky and one is surprised that the film does not show more marked bony changes. The only changes seen may be:

(1) A slight decrease in bony density.

Fig. 4 (*left*). Same case as shown in Figure 3, after treatment.

Fig. 5 (*right*). Same case as shown in Figures 3 and 4, lateral view, after treatment. Patient alive and well at this time, six and one-half years after first treatment.

(2) The medullary canal may be very slightly widened.

(3) Slight changes in the periosteum and thinning of the cortex.

Fig. 6, Case 4. Section reported by Ewing. Endotheliomyeloma of os calcis, a common location for this tumor.

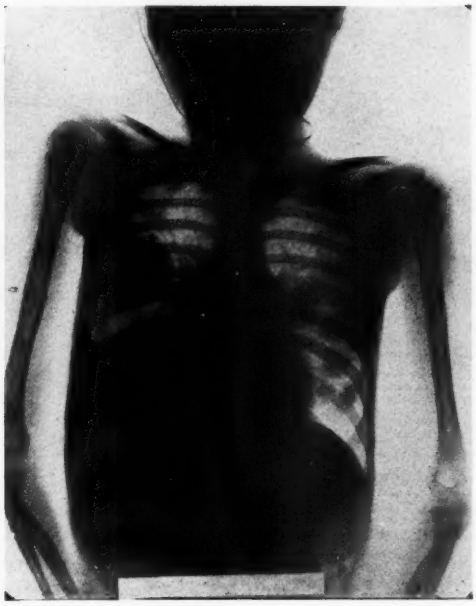

Fig. 7. Same case as shown in Figure 6, showing metastasis to lungs.

(4) The process usually involves, in the case of the long bones, a large portion of the shaft, frequently from one-third to two-thirds of its entire length.

As time goes on, the above changes become more pronounced and a definite diagnosis from the film alone can be made, for in the typical and well-developed case the roentgen-ray features are quite striking and characteristic.

I recall seeing the films of a case sent to me for a roentgen-ray examination and diagnosis, which probably was one of the first which led Dr. Ewing to his investigation, resulting in the description of a tumor entirely new in medical literature.

The tumor involved the upper two-thirds

Fig. 8, Case 5. Showing similarity to Case 4. Endothelioma of os calcis before treatment.

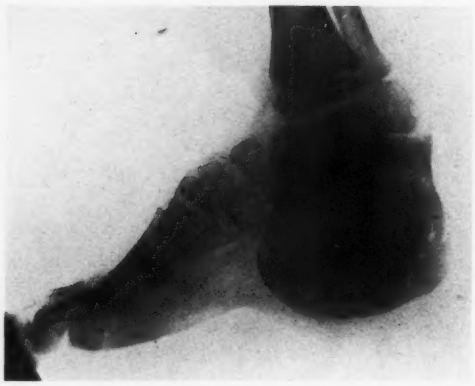

Fig. 9. Same case as shown in Figure 8, showing result of roentgen-ray treatment. Patient alive and well, with no evidence of disease, four and one-half years after first treatment.

Fig. 10, Case 6. Showing recurrence of giant-cell tumor in head of tibia after curettage.

of the shaft of the radius in a girl aged fifteen. There was marked swelling of the forearm, local tenderness and heat. The patient ran a temperature around 101° F. But in spite of the tumefaction of the forearm, the change in the radius was not as well marked as one would expect to find. The medullary canal was slightly widened, the cortex lacked normal density, but there was no localized gross bone destruction or bone production. The periosteum in places, especially at the upper and lower limits of the tumor, was slightly elevated and thickened, but beyond in the soft parts the extent of the tumor was clearly shown.

I was at a loss to classify the process, and, in describing the films to Dr. Ewing, stated that they lacked the characteristic roentgen-ray features of any primary bone tumor with which I was familiar. Some months later, when Dr. Ewing had an opportunity of examining the tumor in his laboratory. he said he believed it to be a tumor, as far as its description in medical literature was concerned, hitherto unrecognized and unclassified.

There probably are no other primary bone tumors which as a class demonstrate more promptly and strikingly the effect of small doses of radium or roentgen rays. Large tumors given 50 per cent of a full skin dose, and frequently only 20 per cent at depths of 5 to 10 cm., disappear completely within a few days. However, the response may be deceptive, and in order to prevent recurrence, extension, or metastasis, heavy doses should be given. It may be that some giant-cell tumors are as sensitive to irradiation as Ewing's tumor, but the effect is not demonstrated as promptly. The reason for this is obvious: in endothelial myeloma there is usually present a bulky, soft-part tumor, easily seen and palpated.

In giant-cell tumors one may obtain, with a large dose, a prompt response, characterized by swelling, redness, and tenderness appearing two or three days following the exposure, but unless this is recognized as a reaction to irradiation, considerable specu-

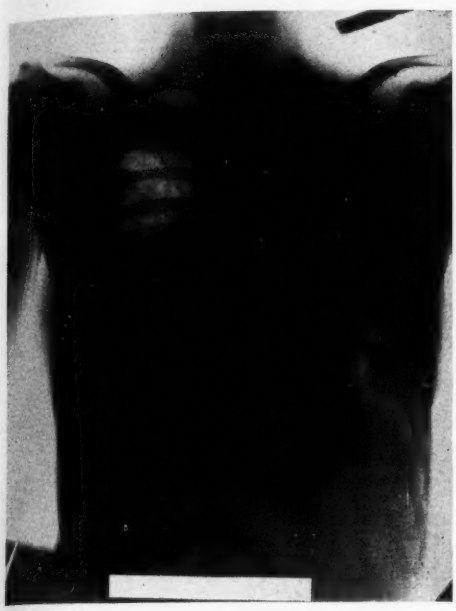

Fig. 11. Same case as shown in Figure 10, showing metastasis to lungs (case of recurrence after curettage of giant-cell tumor in head of tibia).

lation, useless alarm, and recourse to surgery may result from the mistaken belief that the treatment has stimulated the growth. We no longer believe that severe reactions are necessary in order to obtain satisfactory results in the roentgen-ray treatment of giant-cell tumors. We seldom now give a dose even approaching a definite erythema.

Roentgen therapy is commonly applied with the so-called low voltage apparatus and technic, a maximum 10-inch back-up spark, or, probably, to state it more accurately, 125 K.V. peak, 4 ma. of current, 4 mm. aluminum filter, a 10- or 12-inch target-skin distance, depending on the case, and 6 or 12 minutes' exposure.

It is, of course, obvious that the dosage in the roentgen-ray treatment of giant-cell tumors must vary with the case, just as it does in the irradiation of other tumors, and the factors stated in the beginning must all

Fig. 12, Case 7. Giant-cell tumor of radius, before roentgen-ray therapy.

be taken into account in determining the dose and its repetition.

We have stated that the age of the patient is as important a factor as the character of the tumor, but the location of the tumor seems to be of hardly less importance. I want to emphasize the significance of location, and record here an observation bearing on the point which has been re-

Fig. 13. Same case as shown in Figure 12, showing reaction following a heavy dose of X-ray.

peated several times in the last few years. In 1923 an article by Stone and Ewing appeared in the *Archives of Surgery* entitled "An Unusual Alteration in the Natural History of Giant-cell Tumor of Bone." I was so impressed with the developments in this case, with which I had something to do, that each succeeding case, if at all similar, has been followed closely, and there have been an average of two or three such cases each year since then, which have come to my attention. The location of most of these tumors, as was the one reported by Stone and Ewing, has been the head of the tibia. The roentgen-ray and histologic features were typical of benign giant-cell tumors, but why such a large percentage of these tumors, located here, recur after curettage is not clear.

The density of the bone in which the tumor occurs, its contour, whether or not it is subject to great pressure or strain, together with the density and bulk of the surrounding soft parts are probably the important factors which make the location of a giant-cell tumor of significance in estimating its response to irradiation.

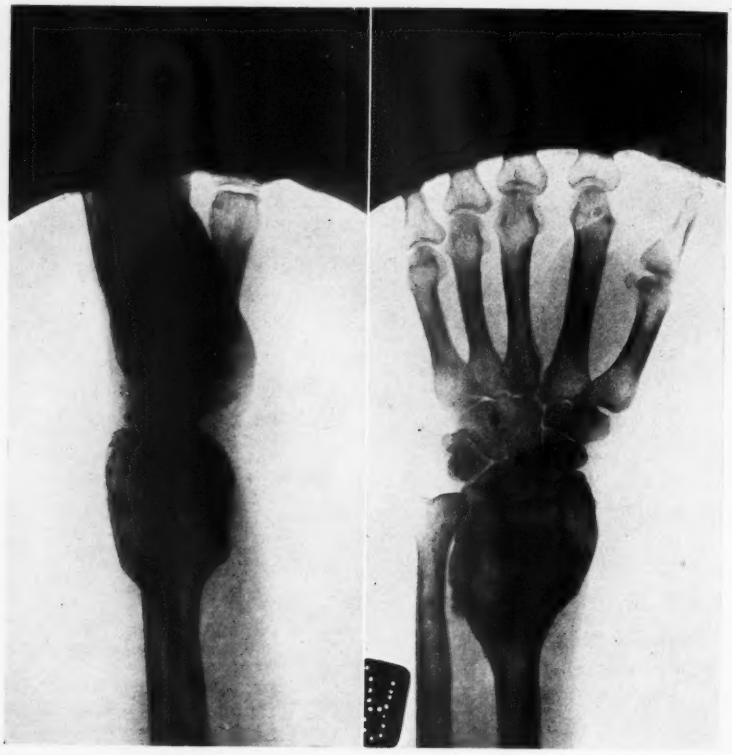

Fig. 14. Same case as shown in Figures 12 and 13, showing process of bone repair after reaction subsided.

In those instances where giant-cell tumors have become malignant and caused the death of the patient, the large majority have been located in the head of the tibia, and the treatment has been the method advo-

Fig. 15, Case 8. Showing giant-cell tumor recurrence after curettage and before roentgen-ray treatments.

Fig. 16. Same case as shown in Figure 15, showing reaction to heavy irradiation.

Fig. 17. Same case as shown in Figures 15 and 16, showing repair after reaction had subsided.

cated by Bloodgood, *i.e.*, curettage, so that in these cases there were present factors, other than location, having considerable significance. They all had curettage—and in some instances two or more times—for the recurrences. Some of the tumors became infected; in some, the recurrence fungated through the incision. External radiation was employed more or less ineffectually in some, and radium buried in others, to control the recurrences. The metastases to the lungs, which occurred later and were re-

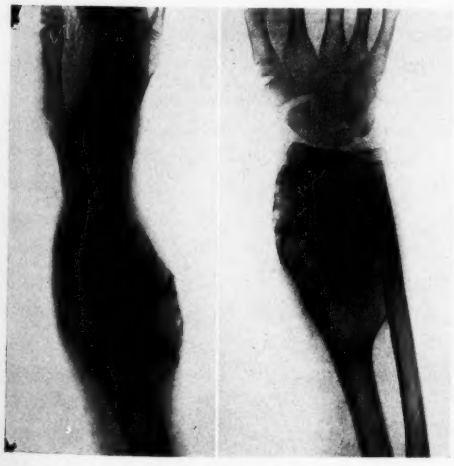

Fig. 18, Case 9. Showing giant-cell tumor after second recurrence following curettage, with bone transplant (absorbed).

Fig. 19. Same case as shown in Figure 18, showing repair process following light doses of X-ray. No reaction, such as shown in Cases 7 and 8, was obtained.

Fig. 20, Case 10. Giant-cell tumor, before roentgen-ray therapy.

Fig. 21. Same case as shown in Figure 20, lateral view.

Fig. 22. Same case as shown in Figures 20 and 21, after light doses of X-ray. Patient followed occupation during period of treatment; was not confined to bed or hospital; used walking Thomas splint—crutches later.

Fig. 23. Same case as shown in Figures 20–22, after roentgen-ray therapy, showing repair. Note preservation of joint surface. The functional result was perfect—no limitation in motion.

vealed by the roentgen films, were similar to those noted in osteogenic sarcoma.

The lesson to be learned by the surgeon from these cases, or, to state it in another way, the warning for the roentgenologist to give the surgeon, is that if he must persist in the curettage of giant-cell tumors in spite of the evidence accumulated to date of the advantages of the roentgen ray, his chances for success in the curettage of giant-cell tumors of the head of the tibia are quite definitely less than at the lower end of the femur.

Judging from the number of patients with giant-cell recurrences following curettage sent to the Memorial Hospital, one is led to believe that the method of treatment advocated by Bloodgood, *i.e.*, curettage, does not yield the high percentage of cures credited to it by its followers.

When these failures after curettage occur, with recurrence of the tumor, metastasis, and death, the surgeon shrugs his shoulders, shakes his head, reads the roentgenologist's report, quotes the pathologist, and says: "You see, they can't tell the difference between the benign giant-cell tumors and the malignant." He cannot quite understand that his method of treatment has been responsible for the transition from a benign to a malignant tumor, and that giant-cell tumors in certain locations may undergo this transition more readily than in others. He fails to realize that, no matter how carefully he goes about the curettage, or how skillful he may be with his hands, he is sure to damage or destroy the mechanical barrier placed about the tumor by the tissues, and that it is this mechanical barrier, present to a greater or lesser extent in every case, and shown in the radiographs as a dense white line, which determines to a large extent the degree of malignancy and the effort at growth restraint.

With this barrier damaged or destroyed, it is not difficult to picture the ease with

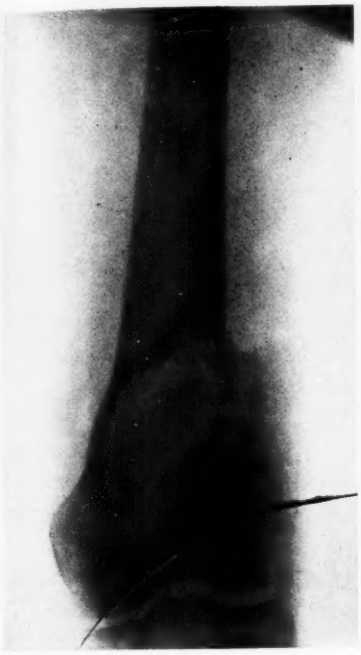

Fig. 24, Case 11. Giant-cell tumor, aggressive in character. Section reported by Ewing.

Fig. 25. Same case as shown in Figure 24, after roentgen-ray therapy, showing callus-production. Bone regeneration noted. Functional result perfect, and no evidence of the disease noted at this time, five years after first treatment.

which a few tumor cells which may be left behind invade the tissues or are let loose, to be taken up in the blood stream and lodged at some distant point, as in the lungs.

But what about the failures of the radiologist? We have them, of course, and unless he not only has an adequate working knowledge of physics, and is also thoroughly familiar with the clinical behavior of tumors and their varying responses to various doses of radium or roentgen ray, the failures will inevitably increase, and the method will fall into disrepute.

This brings us back to the question of dosage, and I would like to warn against the use of heavy doses in the roentgen-ray treatment of giant-cell tumors. Not only may heavy doses be followed by severe, unnecessary reactions or pathologic fractures, but, more important, bone regeneration may be retarded. If this method of treating bone tumors is to survive, the period of disability following irradiation must be shortened, not lengthened, as compared with the period of disability following curettage.

Callus-production will speedily follow destruction of the tumor, provided the dose employed to destroy the tumor has not also damaged the mechanical barrier and the normal tissues about it. But giant-cell tumors occur in locations where callus-production is slow, and if this is combined with advanced age, consideration must be given

Fig. 26, Case 12. Giant-cell tumor involving ilium, ischium, and pubis, before irradiation.

to the feasibility of some such surgical procedure as excision and implantation of a bone graft.

What is the minimum dose, therefore, capable of destroying the tumor? Of course, this question can be answered only when the factors stated in the first part of the paper are submitted and considered.

In the treatment of osteogenic sarcomas there appears to be evidence that pre-operative irradiation is of some value. It has been noted that, following a series of fairly heavy roentgen exposures, films made from time to time demonstrate a definite attempt at ossification, limitation, and encapsulation of the growth. The period during which this has reached its height, and during which the tumor is comparatively benign, can be estimated only by a study and comparison of films made at intervals of several weeks, combined with the physical findings. It is during this period of comparative quiescence and encapsulation of the tumor that amputation may be followed by a better chance of cure.

In conclusion, I believe we are justified in assuming from the data accumulated to date that the roentgen-ray treatment of giant-cell tumors has passed the experi-

Fig. 27. Same case as shown in Figure 26, after irradiation. Patient alive and well, with no evidence of the disease, ten years after first treatment.

Fig. 28, Case 13. Giant-cell tumor of the ischium, before roentgen-ray therapy.

Fig. 29. Same case as shown in Figure 28, showing callus-production and bone regeneration, following roentgen-ray treatment. Functional result perfect. Patient alive and well, with no evidence of the disease, eight years after treatment.

Fig. 30, Case 14. Rapidly growing, aggressive, giant-cell tumor, before roentgen-ray therapy.

Fig. 31. Anterior view of same case shown in Figure 30.

Fig. 32. Same case as shown in Figures 30–and 31, showing prompt bone regeneration following several small doses of X-ray. This patient lost no time from his occupation of travelling salesman during treatment, using a crutch and a cane, but no splint.

Fig. 33. Same case as shown in Figures 30–32, demonstrating rapid repair following a few light doses of X-ray. Note condition of joint surfaces.

mental stage, and, with but few exceptions, the results in general from every angle are far superior to those secured by surgery.

Continued advancement in the irradiation therapy of malignant bone tumors will be hastened or delayed, depending on the radiologist. The degree of co-operation he will receive from his colleagues depends almost entirely upon his ability to demonstrate the superiority of his method of treatment. The success or failure in the treatment of every case will depend largely upon his ability to recognize the limitations of irradiation therapy.

FACTORS IN DOSAGE DETERMINATION IN INTERSTITIAL RADIATION[1]

By HAYES E. MARTIN, M.D., Assistant Attending Surgeon, Memorial Hospital, New York

FROM a technical standpoint, radiation therapy may be divided into two general methods, namely, external and interstitial. The purpose of both methods is to produce within living tissue the identical biological effect. In certain instances either one may be indicated to the exclusion of the other, but, in general, they are complementary and offer two technical means to the same end. Ordinarily they can best be utilized when employed together. The present discussion deals exclusively with the problems of dosage in interstitial radiation and, therefore, the advantages of external radiation as an important adjunct have been purposely omitted.

The determining factor in successful radiation therapy is the "tissue dose" or the quantity of radiant energy reaching all parts of a volume of neoplastic tissue. The term "tissue dose" is not to be confused with the millicurie, millicurie-hour, or milliampere-minute doses. The latter deal only with the physical qualities of the radiating source. Due to the physical nature of the radiations themselves, the tissue dose can not be made uniform or diffuse, and consequently some portions of a mass will always receive many times the intensity of others. This difficulty is very significant in interstitial radiation, with which we are particularly concerned in this discussion. The tissue dose of any mass should, therefore, be considered as of that portion which receives the smallest quantity of energy.

Accurate dosage implies the production, in a neoplastic mass, of the smallest tissue dose sufficient to cause death of all neoplastic cells within it. In order to attain such accuracy, it is essential, first, that we know beforehand the minimum lethal tissue dose of the tumor in question, and, secondly, that we be able to produce at least that intensity in all parts of a given tumor mass.

The difficulties in attaining this ideal are several. Although the comparative radiosensitivity of a neoplasm can be predicted by its general classification and by its individual morphology, there is at present no means of predetermining its minimum lethal dose. The question of dosage in a given lesion is not answered by stating that it is radiosensitive or radioresistant. We are also confronted by the lack of a satisfactory unit for measuring dosage below the surface of skin. At present, the only biological unit of radiation is the skin erythema dose and since the skin reaction varies in the individual and is subject to various interpretations, depending on the observer, it can never be sufficiently definite. In using physical standards, we find the very short (though significant) distances difficult to measure and practically impossible to duplicate in practice.

It may as well be admitted that accurate dosage is not possible in practice, and that at present our best results are obtained by intentional overdosage. A compromise must be made between the larger dose with its assurance of adequacy though accompanied by more discomfort, and the lesser dose with more danger of recurrence but less discomfort. Overdosage in radiation can fairly be compared to other accepted surgical procedures in cancer therapy. An entire breast is sacrificed and the axilla dissected free of all its gland-bearing tissue

[1]Read before the Radiological Society of North America, at the Fourteenth Annual Meeting, at Chicago, Dec. 3–7, 1928.

even though the breast only may show a small mass of carcinoma; and again, a block dissection of the neck may be done in the presence of only one palpable node.

In the face of such considerations as these, the clinician must plan his dosage in a given lesion. To my mind, the admission that dosage determination in interstitial radiation therapy is largely empiric raises no question as to its comparative worth as a method. No doubt further investigation of the physics of interstitial radiation will do much to simplify this problem, but the dosage will probably always remain largely empiric and dependent on the consideration of numerous factors always present in different combinations in the given case.

A list of the most important factors to be considered in the estimation of interstitial dosage may be tabulated, as follows:

1. Size of the lesion.
2. Shape and contour of the lesion.
3. Radiosensitivity of the neoplasm.
4. Tolerance of the adjacent normal tissue and the effect on the whole organism of a lessened function of this tissue.
5. Tolerance of the organism as a whole.
6. Variation in the physical characteristics of the implants, such as their number, position, filtration, and strength.
7. Previous radiation or intended external radiation.

These factors will now be discussed singly and in order.

1. *Size of the Lesion.*—The size of the lesion will obviously be one of the most important considerations in the determination of total dosage. From the practical standpoint, this does not cause great difficulty in the smaller masses (below 2 cm. in diameter) even of the most radioresistant character. In these small masses, several times the required dose may be employed with no disadvantages. The total amount of tissue irradiated even with overdosage is relatively small in comparison to the organism, and any slough of adjacent tissue will be absorbed without difficulty.

An examination into the physics of interstitial radiation will disclose, however, that a dose sufficient to overdose several times a mass 1 cm. in diameter may be too small, or barely sufficient, to cause regression of a mass 2 cm. in diameter. The relative amounts of radon in implants necessary to produce equal tissue doses in various sized masses is shown in Table I.

TABLE I

Diameter, cm.	Dose, mc.	Diameter, cm.	Dose, mc.
1	1 *n**	4.0	22 *n*
1.5	2.5 *n*	4.5	30 *n*
2.0	5.0 *n*	5.0	38 *n*
2.5	7.5 *n*	5.5	48 *n*
3.0	11 *n*	6.0	60 *n*
3.5	16 *n*		

The dosage requirement is seen to multiply more than as the square of the increased radius.

A concrete example will illustrate the difficulty in estimation of dosage for larger masses. Suppose it has been found that, in a certain histological type of squamous carcinoma, a node 2 cm. in diameter will always be destroyed by 8 millicuries in gold implants. This may possibly be more than absolutely required but it has been found to cause no troublesome sequelæ. Suppose, then, that a mass 4 cm. and another 8 cm. in diameter of similar nature are encountered. What amount of radon must be implanted to produce an equal tissue dose? We are able here to give definite figures based on a previous investigation. The 4 cm. node would require 40 millicuries and the 8 cm. node 176 millicuries. The latter dose is out of the question, as it is obviously more than required and far beyond the limit of safety. It seems certain that we habitually overdose smaller masses with

*The figures in the last column are expressed in multiples of *n*, which stands for an arbitrary millicurie dose.

impunity, and rightly so, if the results are satisfactory. Furthermore, an appreciation of Table I might help to explain the often discouraging results in the treatment of the larger masses. Any clinician who has used large amounts of radon interstitially will appreciate that there is a limit to the size of a safe dose and, therefore, to the size of a mass which can be heavily and successfully treated with interstitial radiation.

2. *Shape and Contour.*—As the radiations from an implant are emitted from a point source for all practical purposes, the zone of any given intensity about one implant is spherical and, therefore, for a small spherical mass, the problem obviously is simply to place one implant at its center. For larger, irregular, or flat lesions, the problem is more complex.

In a series of experiments reported (1) before the American Radium Society at Minneapolis in June, 1928, we studied the distribution of intensity surrounding multiple implants differently spaced, and calculated the most efficient placement in spherical and irregularly shaped masses. Here it was demonstrated that as the possibilities of variations in shapes of masses and of spacing and arrangement of implants are infinite, no practical special rule can be worked out for the treatment of irregular masses. In any arrangement of several implants, each must be considered as a unit contributing its zone of therapeutically irradiated tissue to the total irradiated mass. The intensity is strikingly localized to the neighborhood of each implant. To consider that a number of irregularly spaced implants are mutually benefited in their individual zones of action is an error. The action of a group of neighboring implants is actually a sum of adjacent or coalescing units about each implant.

From these experiments, we demonstrated that a spherical mass is equally as well irradiated by a given quantity of radon from one point at the center as from any number of points distributed throughout the mass, however placed. On the basis of this fact, we find it of advantage to consider all masses to be treated with interstitial radiation either as spheres or as combinations of spheres. A slightly irregular mass is considered as a sphere whose diameter is equal to the longest axis of the mass in question; a more irregular, or flat mass as a combination of adjacent or overlapping spheres; as, for instance, a flat lesion in the floor of the mouth 4 by 1 cm. will be considered as four or five overlapping spheres. Each one of these hypothetical spheres will be treated with its implant. Calculations will prove that implant No. 1 adds only an infinitesimal portion to the zone of action of implant No. 5, and that each separate implant will irradiate its local zone just about as well alone as with the assistance of the others (Fig. 1).

3. *Radiosensitivity of the Neoplasm.*—The exact nature of the mass to be treated is of great import in dosage determination. That there is wide divergence in the radiosensitivity of neoplasms needs no particular emphasis. The determination of the nature of a growth rests mainly on its histological study although the history and clinical features are both of assistance. The exact quality which is responsible for the radiosensitivity of a neoplasm is unknown, but, in general, it seems to depend on its differentiation from the embryonic form. Broders' classification here serves as an index within particular classes. Vascularity, rapid growth, and soft consistency also indicate radiosensitivity. The individual morphology of the cells often permits the pathologist to predict that a lesion will respond to a small dose although its structure gives no clue as to its origin.

Several classes of neoplasms seem to behave rather uniformly in response to radiation, as, for example, the radioresistant melanoma or neurogenic sarcoma and the radiosensitive lymphosarcoma. But in most other varieties, the exceptions are so numer-

ous as to emphasize the unreliability of any one known sign of radiosensitivity. Hard non-vascular papilloma of adult type has been seen to regress completely within a few days under moderate dosage. Intra-oral transitional cell epithelioma which is ordinarily radiosensitive, is at times found to be quite radioresistant. Occasionally the primary lesion and a neck metastasis will be found to react differently. Again, the entire range of radiosensitivity of intra-oral squamous carcinoma seems to be found within Broders' Group II. Many neoplasms can ordinarily be identified clinically with sufficient accuracy for outlining treatment, as, for example, carcinomas of the breast and sarcomas of bone. Lesions of the upper air passages, oral cavity, esophagus, rectum, uterus, vagina, etc., present no difficulties in securing tissue for histological examination. Opinions differ widely as to the justifications for biopsy. At the Curie Institute in Paris no case will be treated without biopsy. In general, it is believed at Memorial Hospital that a biopsy should be obtained in all cases where no incision through normal tissue is necessary; and where such is not possible, the question is determined in the individual case.

While it is obviously more simple to obtain regression of a radiosensitive lesion by irradiation, the ultimate result often depends a great deal upon the natural course of the disease. As a general rule, the more radiosensitive neoplasms tend to metastasize more widely, outside or beyond their direct neighboring lymphatics. This is characteristic of the radiosensitive transitional cell epithelioma. The average squamous carcinoma of the intra-oral group tending toward unilateral metastases offers perhaps a better prognosis even though more radioresistant. The extremely radiosensitive lymphosarcoma is notorious for its variable and widespread metastasis. The field for radiation lies mainly in that group of tumors which is more radiosensitive than normal tissue.

Ordinarily the dosage will depend on the radiosensitivity of the neoplasm, although at times the local and general tissue tolerance will not permit a dose sufficient to care for the larger and more radioresistant growths.

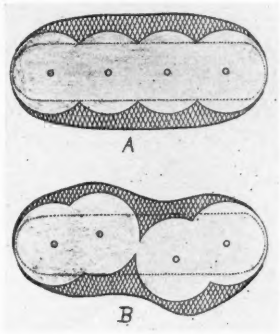

Fig. 1. (*A*) A schematic representation of 4 gold seeds inserted into a flat lesion which is represented by the dotted line. The clear portion represents the outline of a hypothetical therapeutic dose if each seed is considered as a unit receiving no assistance from its neighbor. The cross-hatched area indicates the limits of this hypothetical dose as it actually occurs, due to the complementary action of the several seeds. It will be noted that at the ends the complementary action is so small that the unit action of the end tubes is not increased to an appreciable degree by any assistance from the others. (*B*) Represents a slightly askew arrangement of 4 seeds.

The dosage may be influenced by a converse argument. The more radioresistant neoplasms may be impossible to treat successfully in the large masses. A dose sufficient to cause their regression might not be tolerated by the organism as a whole, while an equal sized mass of a radiosensitive growth might be well cared for by a dose safely tolerated by the patient. Such a radioresistant mass may be reduced in size and retarded in growth by a smaller dose,

while a radiosensitive mass of equal size may be entirely eradicated by a larger dose although attended by more immediate discomfort.

4. *Tolerance of the Adjacent Normal Tissue and the Effect on the Whole Organism of a Lessened Function of this Tissue.*—There are certain limits beyond which it seems unsafe to go in dosage in certain localities. For instance, the tongue and the floor of the mouth can not be safely irradiated with much over 40 millicuries in the average case. The comparatively distant effect of such doses on the larynx and intricate mechanism of the neck as a whole may not be compatible with life. When implants are placed near the surface of either skin or mucous membrane there is a tendency toward ulceration and a complicating mixed infection. This tends at times to counterbalance the benefit derived from a larger dose.

On the other hand, larger doses are well borne in some parts, as, for instance, a limb or the breast. The esophagus, due to its thin wall and immediately adjacent delicate structures in the mediastinum, does not well tolerate even the smaller doses. The orbit, except for the supervention of cataract, seems to tolerate a considerable intensity.

Even though some adjacent structure be interfered with or destroyed by close proximity to buried implants, it may be well to consider whether they can be partly or wholly spared, compatible with fair comfort. In this category come cartilage and bone in the various parts of the body, or the testicles and ovaries.

5. *Tolerance of the Organism as a Whole.*—Large doses (100 millicuries) of interstitial radiation are usually followed by a noticeable effect on the general health, aside from the malnutrition and sepsis which are so much a part of the disease itself. There may be a definite fall in the red blood cell count and hemoglobin, probably both from a direct action on the blood cells and from an indirect toxemia due to toxic substances liberated by the action of radiation on other cells. With external radiation the outlying parts of the body can be shielded to prevent a large part of this body dose, but it must be admitted that there is no possible means of protection from a deeply placed buried source. Massive doses of interstitial radiation in exposed ulcerated lesions are commonly attended by a long period during which a large mass of devitalized tissue must be absorbed or extruded by sloughing. During this period, sepsis is a common complication. If after a large dose, this condemned mass of tissue be excised (surgically if at a depth and with a cautery if at the surface), convalescence can be made much shorter and more comfortable. Of this category, the antrum and the tongue are important examples. Where sepsis is a serious factor even at the beginning, we are inclined to excise the condemned mass after a five- to ten-day period of interstitial irradiation. In ten days about 84 per cent of the radon has been destroyed. Dosage, in such cases, is computed on the basis of the daily rate of decay of radon (Table II). This elimination of the already condemned and intensely irradiated tissue permits a tolerance of larger doses.

6. *Variation in the Physical Characteristics of the Implants.*—The elimination of beta radiation by the use of filtered implants has been of great importance in interstitial radiation therapy. Before their development, the intensely localized effect of beta radiation from unfiltered implants was a stumbling block in the successful use of interstitial therapy.

The implants now used at Memorial Hospital have a filter of 0.3 mm. gold which eliminates about 97 per cent of the beta rays, and our dosage calculations are based entirely on this filtration. While beta radia-

TABLE II

CALCULATION OF DOSAGE DELIVERED BY RADON IMPLANTS LEFT IN FOR TEN DAYS OR LESS

Time (days)	Strength of implants in radon units	Millicurie-hours per radon unit	Total millicurie-hours delivered per radon unit
1	1.000	21.9	21.9
2	0.8353	18.3	40.1
3	0.6977	15.3	55.4
4	0.5828	12.8	68.2
5	0.4868	10.7	78.9
6	0.4066	8.9	87.8
7	0.3396	7.5	95.3
8	0.2836	6.2	101.5
9	0.2369	5.3	106.8
10	0.1970	4.2	111.0

tion has a distinct advantage in the treatment of very superficial surface lesions, we believe that its feeble penetration offers little benefit interstitially and that is highly disadvantageous in that it increases the volume of slough. The use of filtered implants permits greater dosage of penetrating gamma radiation.

Not only is the number and position of supreme importance in securing a proper distribution of intensity, but the approximation to the ideal in these aspects will determine the necessary dosage. It may as well be admitted that it is not humanly possible to place implants exactly, even though their theoretically correct position and spacing could be predetermined in each individual case. If the implants are not correctly placed they will be less efficient and the dosage must therefore be larger. Due to this human factor of error, we must deliberately overdose, or at least admit that we have done so in previous successful cases, unless we happily and accidentally placed the minimum doses in exactly the correct positions and arrangements.

As we have previously shown (1), a sphere is equally and as efficiently irradiated from one point at its center as from multiple points properly spaced. There is, however, as we have also shown, a greater volume of slough in the single implant. Should the mass be composed of a sphere of neoplastic tissue, a correct dose will cause regression of the mass and its absorption before slough can form at its center. It is obviously impossible often to secure single implants to fit the various sized masses except the smaller, but physical calculations show that implants should be placed within the outer third of the radius of the sphere of tissue which they are intended to irradiate. If this is done they will irradiate such a sphere equally and as efficiently as if placed at its center.

7. *Previous Radiation or Intended External Radiation.*—Each succeeding failure entirely to eradicate a neoplasm by irradiation renders the next attempt more difficult. This is mainly due to a lessened tolerance and lessened power of regeneration of the local normal tissue. Normal tissue subjected to an average therapeutic dose never quite regains its former tolerance, and this tolerance decreases progressively with each succeeding irradiation. Although opinions differ, there seems to be a "vaccination" of neoplastic tissue by sublethal doses so that it becomes progressively more radioresistant with repeated irradiation. The beneficial effect of several applications at long intervals is not cumulative except for palliation or for the treatment of benign processes such as hemangioma, where a slow fibrosis is the aim. In planning dosage, this lessened tolerance of the local tissue must be taken into consideration at any time after the preceding acute reaction has subsided.

External radiation can practically always be combined with interstitial to good advantage, as the most serious drawbacks of each method are widely different. In the former, the skin and superficial tissues must be considered, while in the latter the local or immediately adjacent tissues suffer most.

When used together, the dosage of each will depend on the possible comparative advantage of the other.

Conclusions.—A consideration of the many factors involved indicates that dosage determination in interstitial radiation therapy is empiric and that it will probably always remain largely so. The proper evaluation of these factors in each individual case makes careful clinical observation of supreme importance. Successful dosage and the correct interpretation of its clinical effect necessitates at least an elementary knowledge of the physics of interstitial radiation.

SUMMARY

1. The determining factor in successful radiation therapy is the production of a lethal tissue dose in all parts of a neoplastic volume of tissue.

2. The dosage in interstitial radiation is empirical and depends on the proper evaluation of numerous factors always present in different combinations in a given case.

3. These factors are enumerated and discussed separately.

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DISCUSSION

DR. FRANCIS CARTER WOOD (New York): No other institution in this country, scarcely any in the world, could bring to us the vast body of experience, both scientific and clinical, that is offered by the Memorial Hospital group. It is obviously impossible to discuss in any sense all the papers, but there are some points in some of the purely scientific parts that I would like to discuss, and I will leave the strictly clinical side to the other members of the discussing force.

I was very much interested in Dr. Failla's paper. It seems to me it is the best argument that I have heard for my own paper, asking for a simple ionization chamber standardized in biological units for the general worker in X-ray. We who have ample facilities do not realize the difficulties under which the man in a small town has to carry on his radiotherapy. It has been brought to me forcibly by letters which I get from all parts of the country, either from patients or physicians, saying, "My patient is suffering from a condition which could be palliated, or possibly cured, by radiation." When I look on the map I find that that patient is one or two hundred miles from any center where X-rays can be applied. I write and ask if there is any radiographer in the town, or anywhere near, and often learn that there is no one near. It ought to be possible to give radiotherapy to a much greater extent than is now practicable in the United States. If even the man who is doing only radiography, who knows little about radiotherapy, could be equipped so that he would not do damage, we could refer these patients to someone who could benefit them, even though his knowledge of radiotherapy were not very great.

Until there is some method whereby we can supplement the work of the man who has not had experience in a large institution, or other opportunities, we are very much limited in the treatment of cases of cancer. Surgery is better distributed than radiation in this country. Good surgery is available in many places. Good radiation is available to a much more limited extent. Until that situation changes (and the only way to change it is to give the man an accurate means of measuring the output of his machine), we will not be able to extend the benefits of radiation to the entire population.

Dr. Failla is perfectly correct in his statement about the insufficiency of mere milliammeter-voltmeter readings, and there is one point to which I may call attention in this connection. While I entirely agree with

him, yet no one can establish all the criteria he has laid down without more facilities than most of us possess. Also, those who are using the machines of the kenotron rectifying types must be very careful, because those machines deliver a larger quantity of X-ray with the milliammeter and voltmeter readings than the mechanically rectifying types. With a completely smoothed current the biological effect on cancer cells is twice that of an ordinary mechanically rectified machine using only the spark gap and the milliammeter readings.

The explanation is perfectly simple; with mechanical interruption the tube is resting half the time, whereas, with a perfectly continuous current the tube is delivering X-ray all the time. But the milliampere readings and voltmeter readings will be the same, and the modern, practical kenotron rectifying machine delivers a dose somewhere between the two. So here, again, is a definite evidence that you cannot rely wholly upon these two simple meter factors.

Dr. Quimby has brought up a question which to me is very interesting. Those of you who heard me read a paper at this meeting may remember that I showed that if one exposes flies' eggs to 50 per cent of X-ray and 50 per cent of radium, he gets a 100 per cent dose; Dr. Quimby gets 130. The explanation of the difference I am not prepared to offer, but it must lie somewhere in the difference of reading an erythema dose. If 30 or 40 per cent more radiation can be given without changing the erythema very much clinically, then the difference in our results must lie in that variation, whatever it is. If we can do what Dr. Quimby says, there is a great advantage in mixing our types of radiation, but biologically on individual cells we do not see this phenomenon—that is, two and two still make four, so to speak. A 50 per cent dose of X-ray and a 50 per cent dose of radium will give a 100 per cent dose on flies' eggs.

Dr. Ewing's discussion is one which is profitable to all of us, and I think he guarded his statements sufficiently by protesting against any assumption of mathematical accuracy in his opinion.

The classification of tumors is immensely valuable, but it carries with it a little danger.

Only a short time ago I saw a patient whose tongue had been partly removed and there was a recurrence in the neck. I wrote the physician who referred the case to me and said, "I shall be glad to give the man palliative radiation to check the recurrence." I had a letter back in the next mail saying that the tumor belonged to Broders' classification No. 2 and, therefore, was sensitive to radiation. Unfortunately, the case did not agree with that classification and the tumor has been resistant.

We must not let the surgeon think that because he knows Broders' classifications he can tell us a given case can or cannot be cured, or, what is more important, he must not tell the patient that a given case of Broders' Class 1, 2, or 3 can necessarily be cured by radiation. Because if that is done criticism will fall on the radiologist who is unable to cure the case. We know that, unfortunately, tumors of exactly the same histology are sometimes sensitive and sometimes resistant.

Dr. W. H. Woglom published some years ago an article on some interesting experiments, but it was buried in a scientific journal which no one reads. He took three breast tumors from the same mouse and grafted a couple of hundred mice with these tumors. These tumors cannot be distinguished morphologically, yet one group took in about 85 per cent of inoculations, another in 50 per cent, and another in 8 per cent. Therefore, there were three tumors of the same animal in the same organ. Radiation of such tumors shows that they have entirely different radiation suscepti-

bility. Therefore, we must always regard morphological classifications as useful, but not as final. Take, for example, lympho-epithelioma. In a recent case the tumor was no more radiosensitive than the usual squamous-cell tumor of the neck. On the other hand, a case of lympho-epithelioma of the tonsil yielded to very moderate radiation. The morphology of these two tumors was very much alike. There is evidently something that we know nothing about, and all we can say is: there are different biological qualities in the tumor cells which upset all of our calculations.

Fortunately, this is not generally so, yet Dr. Herendeen and Dr. Ewing both spoke of the round-cell sarcoma, so-called Ewing's tumor, as sensitive; but in a patient, a man of about sixty, who had one of these tumors in his pelvis, radiation produced absolutely no effect on the growth, not even palliative, for it did not stop the pain.

I wish I could be as optimistic as Dr. Ewing is about the beneficial effects of lymphocytes. Most of the lymphocyte illusion is based on the theory of Dr. Murphy, of the Rockefeller Institute, which has largely been refuted. Dr. Murphy worked chiefly with a single tumor which was not very malignant. If you use a tumor of high malignancy which never disappears spontaneously, you get none of the lymphocyte effects; so that while the statements may be true concerning the tumor which he used, nevertheless it is dangerous to generalize from a single type of tumor, and therefore the experimental evidence is very shaky and the clinical evidence also.

I am puzzled to know why, if lymphocytes are so effective, do tumors grow perfectly well in cases of lymphatic leukemia. Why do we see lympho-epitheliomas? Why do tumors grow so well in lymph nodes? Also, why, if the lymphocytes themselves have destructive action, do they not destroy the tumor immediately? We have all seen tumors of many types grow efficiently and effectively with a number of lymphocytes present.

It seems to me that we must not hope too much from lymphocytes. Better hope for a direct killing effect of the X-ray.

As to the "vaccination" of tumor cells by repeated radiation, that problem has been attacked in my laboratory by Dr. Prime, who has rayed a tumor, giving it just a sublethal dose, grafted it into an animal, taken it out, rayed it again with a sublethal dose, grafted it again, thus giving it a chance to live. This has been repeated ten or fifteen times and at the end of all of this radiation of individual cells the tumor is still killed with exactly the same X-ray dose as when we started. So the vaccination factor, we must believe, cannot depend upon changes in the cancer cell itself, but the changes in the surrounding connective tissue. Everyone knows that some tumors which have been repeatedly rayed cannot be influenced further by radiation. If you will examine that tissue you will find it is devitalized, with very poor circulation, nothing to feed the cells of the healthy tissue. Therefore, as soon as you ray such an area, the tissue breaks down and hence it is impractical to treat it.

In that sense we all know that there is some change which forbids repeated radiation, and the full dose should, therefore, be given the first time.

Another evidence of the lack of killing power of the tissues on the cell is seen in the experiments by two German surgeons, in which they exposed the chest of a patient with a cuirasse of the breast through a lead grid. The strips of lead were very narrow, and the tumor disappeared in strips, leaving little ridges of neoplasm where the cells were protected from direct radiation. In other words, these remarkable destruc-

tive effects of the tissues are not evident over a couple of millimeters to one side of an area where the tumor has been destroyed by the direct impact of the X-ray.

I have also done an experiment in which tumor particles were rayed in glass and the lethal dose determined, and then I have rayed the same type of tumor growing in the leg of a rat, and the dose required to kill both sets of cells was exactly the same. In other words, the rat was not able to do anything to help kill his own tumor.

I feel, therefore, that we must have more evidence than we have now that there is some destructive effect of the tissues on the cancer cells before we can argue very much from that point of view.

I do not deny for one moment that the changes in the blood vessels seriously interfere with the growth of the tumor cells. In that sense the tissues do have action, but it is a secondary action, as has been demonstrated by planting a highly malignant carcinoma in the middle of a large rat fibroma. The bulk of this tumor is practically avascular. Malignant cells can remain in the center of such a fibroma three or four months, when under ordinary circumstances the animal would be killed by the growth of the carcinoma within a few weeks. So long as it is encased in this fibrous mass, where the cancer cells get little or no nutrition, they remain inert; but if at the end of that time the tumor is grafted in a fresh rat, the growth will kill the rat promptly, showing that the cells of the tumor have not been altered at all, but merely locked up, so to speak, in a plaster cast of dense fibrous tissue. That is what I think occurs in many of our clinical cases.

You all know the sad experience of doing a biopsy on a case of cancer of the breast, clinically cured by radiation: the tumor begins to grow again. It is also known that occasionally a hysterectomy is done on a patient who has been cured by radium for four or five years and who has been clinically well, and yet in a very few months the patient dies, showing that the operation opened up old lymphatic channels where perfectly virulent cells remained harmless so long as they were shut up.

I think the most important statement made by Dr. Ewing is this—I will repeat it —that the radiosensitivity is not an index of curability. It must be remembered that, while a tumor may be radiosensitive, it may be highly malignant; or it may have a low malignancy and be radioresistant.

Dr. Herendeen referred to the effect of radiation on giant-cell tumors, and I think his point of giving low doses is well taken. With some of these very high doses the bone repair does not seem to take place, and I shall shift in my next few cases and give lower doses to see if I can get more bone repair by not giving so destructive a dose on the bone tissue itself. That is a very important point which I have never before heard mentioned. I could not, however, agree with him on the subject of these giant-cell tumors being stirred up by operation or radiation. One case which he cited was operated on at St. Luke's Hospital, New York. The pathological report was that the tumor was probably an osteogenic sarcoma, and that diagnosis was confirmed by other pathologists. Hence, that particular instance cannot be cited as an example of stirring up the tumor by operation. In this case the tumor was already malignant, though its morphology was very close to what we call benign giant-cell tumor. Also, I feel that one of the cases which he cited, the osteogenic sarcoma which was rayed for six months, then operated upon, but is still well, has another explanation. I would rather say that, in spite of the fact that the patient was radiated for six months, he was fortunate enough not to have metastasis to

the lungs during that period. I doubt if any benefit was obtained by radiation.

It seems to me that as we know these osteogenic sarcomas are with difficulty cured by anything, either surgery or radiation, we should treat them in a different fashion. If you want to give X-ray, I should prefer to give extremely large doses the day previous to the operation. Give ten erythema doses if you want to, and then amputate. Under these circumstances a dose can be given which in all probability will completely sterilize the tumor. Instead, therefore, of giving a course of pre-operative treatments during which at any time a live cell may get off into the lungs and render all treatment purely academic, it would be very much wiser to give what we know is a sterilizing dose and have the patient operated on the next day. The only risk is that the patient may develop bronchitis or pneumonia the next day and the surgeon will refuse to operate; then a severe burn will follow. In other words, when preoperative radiation is done we should do it with a dose that will kill all cells, and then immediately operate. If we give small doses, only a fraction of the cells are killed, and then there is the danger of the distribution of the remainder during the manipulative processes of the operation.

Dr. Henry Schmitz (Chicago): It is obviously impossible to discuss or even to speak of every one of the papers presented in this symposium. I can discuss only a few parts that seem to be of importance, so far as I am concerned.

The experimental findings of Quimby and Pack are of great value, as they will extend the field for radiation therapy.

In the combined method of radium and X-ray therapy, as used in our clinic, it has been empirically found that when radium and X-rays are applied during the same series a higher combined dose may be safely used than with either radiation used alone. We do not hesitate to go as high as 150 to 170 per cent of the erythema skin dose in the combined therapy.

In a recent study with Hueper, our pathologist, on the histologic characteristics of the cancer cell, the cell type, cytoplasm, nuclei, and the stroma, including vascularity, about 250 cases of cervical carcinomas were studied, and the conclusion was reached that high anaplasia was associated with high malignancy and high radiosensitivity.

The end-results of 100 cases were known and plotted according to the degree of histological malignancy. The graph was compared with a similar graph of the good end-results obtained in the clinical groups based on extent of the tumor. We were surprised to find a parallelism between the two graphs. In other words, it was found that a high degree of anaplasia was associated with a high radiosensitivity, but with poor end-results.

Bowing and Fricke have shown the end-results in the four grades of Broders' classification, and their good end-results seem to coincide with ours in relation to the degree of histological malignancy.

Dr. Healy's results are interesting. He finds good end-results in the highly anaplastic carcinomas, which coincides with the findings of Boehm and Zweifel. It will be of great interest to again hear from these various clinics in another year or two, to learn if these contradictory results have changed in any respect.

The contention of Martzloff in one of the recent papers published in the *American Journal of Gynecology*, that it is impossible to determine the true degree of histologic malignancy of a carcinoma from a biopsy specimen, does not agree with the findings of Ewing or the speaker.

I am not prepared to discuss Dr. Adair's

conclusions on the response of the different histological types of breast cancer to radiations. We have been content with the histological diagnosis. The work of Dr. Ewing, Dr. Adair, and Dr. Greenough will guide us in this work. I hope to be able to report in the near future the conclusions we have reached. Dr. Adair corroborated the observation which I reported earlier in this meeting, that localized recurrences show a very high response to radiation therapy, and that even in some fixed local recurrences we had good end-results. This may be due to the fact that the localized recurrence is accessible and practically a superficial tumor.

The Radiological Society of North America owes the Staff of the Memorial Hospital a heavy debt of gratitude for the presentation of this symposium. It is, in my opinion, absolutely outstanding in scientific achievements.

Dr. Henry J. Ullmann (Santa Barbara, Calif.): I believe we are confronted by very much the same problem that Dr. Compton brought up earlier in this meeting. We have two diametrically opposed bits of evidence: one, the tumor experiment with a lead grid, that Dr. Wood cited, and another experiment reported in the London *Lancet*, where two areas were radiated and a tumor planted between them. It grew through the unradiated skin, avoiding the irradiated area.

It appears to me that this is very much like the evidence that X-ray is a wave and that it is a particle, and, therefore, there must be a correlation between two apparently diametrically opposed experiments.

I wonder how we are going to explain the resensitization, following injection of lead, of tumors that have become radioresistant.

Dr. Samuel Brown (Cincinnati, Ohio): I rise in the capacity of an ex-member of Memorial Hospital and I take this opportunity to express my full indebtedness to the Memorial Hospital, and especially to Dr. Ewing. I feel that what I am, and especially what I am not, I owe to that institution.

I wish to congratulate Dr. Ewing on the analysis he presented regarding the sensitiveness of tumors: perhaps, with some exceptions which Dr. Wood indicated, it is a good workable table to follow.

However, I am not fully satisfied with that. If I were to ask you, "Why is this rod more resistant than this pencil?" and you were to say, "It is because the rod is iron and the pencil is wood," that would not be a sufficient answer for me. I would like to know more. I would like to know what are the atoms, the molecules, and the forces which hold these respective objects, which determine their resistance. I would like to know whether Dr. Ewing could enlighten me on this subject and tell me whether a study of the underlying factors would develop a more scientific table in order to determine which tissue or which tumor is more or less resistant to radiation. I think we have to go to the fundamental sciences, such as chemistry and physics, in order to arrive at a more scientific conclusion. To depend upon physiology and pathology of tissues alone is not sufficient to arrive at such a conclusion.

Dr. Albert Soiland (Los Angeles, Calif.): In the fifteen years' existence of this organization I do not believe there has been a more comprehensive and more valuable symposium presented before this body. Every paper is a masterpiece, and when we radiologists can obtain such assistance from a group of specialists from the Memorial Hospital, of New York, we feel that we have been very fortunate indeed.

Out of the mass of evidence presented the apparent fact stands out that radiation

treatment may well be instituted, even when the malignancy grade of the lesion would make the results seem of doubtful value. In other words, if we are to accept the evidence presented by the Canti film and by Dr. Ewing's paper, it seems that we have to come back to our first principle and "kill the cancer cell."

DR. L. R. SANTE (St. Louis): I just want to ask a practical question and make a practical observation. I would like to ask Dr. Ewing, in view of the observation he made on the incarceration of radioresistant cancer cells in heavy masses of dense, fibrous tissue, whether he would consider the surgical removal of such remaining nodules good practice.

I recall that a number of years ago it was uniformly accepted by radiologists and surgeons that such masses should be let severely alone, for fear of the danger of removing the barriers and letting loose these interstitial cancer cells.

Some of the work shown in such instances makes me wonder if this is really so great a danger as it seems. I myself have seen several cases in which fibrous masses such as Dr. Ewing described and such as we have all seen, have developed, have been made inactive for a period of years, and have later been excised (they occurred in locations where they could be completely and widely excised by surgical methods), with complete recovery of the patient.

I would like to ask Dr. Ewing if he has changed his mind in this regard, and what he would consider the proper method.

I would like to make one observation on Dr. Adair's paper, relative to sensitivity of carcinoma of the breast.

We hit upon the idea, similar to the one Dr. Wood spoke of, concerning the overradiation of the part of the breast to be excised. We have done this in a number of cases which have been selected as being particularly suited to this method of procedure, wherein, for instance, there was a rather isolated, well-defined tumor in the breast, with no clinical indication of metastasis in the regional glands. We have taken such a patient, and had the surgeon map out—using silver nitrate stick so as to make a nice black spot on the skin—the full extent of the skin he was willing to sacrifice, feeling that in that way we might treat part of the tumor with a very severe dosage. We have blocked the area with lead and given the patient as high as from six to eight erythemas, using 125,000 kilovolt radiations. Some of these treatments were done years ago. Then we would give that dosage to the patient, with the area blocked out completely with lead, so that none of the black line showed, and within the hour, so that she could not refuse operation, taken the patient to the operating room and instructed the surgeon not to leave any of the black line. In that way you have assured yourself that every part radiated has been removed. We have had a rather consistent observation of a sort of putty-like discharge from the wound, if there has been any drainage, but a prompt healing. We have given radiation so intensive that we have produced pleurisy. Of course, the regional glands were treated with an ordinary preoperative dose, such as you ordinarily would give in high voltage therapy.

The interesting observation we have made in these cases, and one that has been very annoying, to say the least, has been that in every one of these cases, without exception, the patient has developed an extensive carcinoma in from nine to twelve months, approximately. I have no explanation, but merely point the observation as being an interesting thing, and I would welcome an explanation. I may say that the carcinoma produced was absolutely radioresistant.

There was no effect from very large

doses of radiation, even though they were right in the skin. Biopsies showed cancer cells in great numbers in the lymphatic spaces in each instance, and the area covered after a time went beyond the area radiated. The type of carcinoma reported by the pathologist was in each instance, as I recall it, adenocarcinoma.

DR. JAMES EWING (closing): In reply to the specific question asked me by one of the discussants as to whether one should excise the tumor in the particular instance referred to, I would say, as a pathologist, that it would be perfectly safe to excise those things if you thought you could get them all out.

In regard to the significance of lymphocytes, I prefer to emphasize the importance of body reaction over direct killing of tumor cells, as the best principle to follow in radiation therapy, but I am not assuming for a moment that it is good radiation therapy to stir up tissue reactions without injuring tumor cells. The severe injury to the tumor cell is what starts the tissue reaction, and I think it has been proved that the cure of cancer is, as a rule, the combined result of injury—sometimes actual killing—of tumor cells, followed by body reaction to complete the cure.

How can you explain the almost complete failure of reaction in cachectic subjects? Here we have tumor cells, but the tissue response is not adequate to bring about a cure.

I am not willing to adopt the theory that the only way to cure cancer is to cause tissue reaction. I maintain the position that it is unwise to go to the other extreme and say that the only object of radiation therapy is to kill tumor cells.

In regard to lymphocytes, that is a theoretical point. My experience with the microscope indicates that under a great many circumstances the tissue reaction caused by radiation, which is effective in removing tumor tissue, is marked by a considerable degree of lymphocytic infiltration, and I think that the lymphocyte is a factor of importance in that reaction. Of course, the reaction is not successful as a rule. Nevertheless, in the local removal of these tumor cells, growing under ordinary conditions, I find it impossible to avoid the conclusion that the lymphocyte plays an important—although usually unsuccessful—part.

DR. OTTO GLASSER (Cleveland, Ohio): I should like to say a few words in regard to Dr. Failla's paper. For the past six years I have presented papers on radiation dosage at the annual meetings of your Society. If I refrain from doing so this time, it is not because I feel as pessimistic about the situation as Dr. Failla does, but because I feel that the dosage methods have been pretty well established for the time being. We realize, of course, that the only place for the center of standardization of the X-ray dose is the Bureau of Standards, in Washington, but we must not forget that previous work done by a number of research workers in this field has led to the adoption of the international r-unit in Stockholm last Summer, as well as to the working-out of a number of valuable dosage methods which have proved their practicability in the hands of radiologists. It is true that these dosage instruments which are on the market are expensive for the average radiologist to buy, but it is because only a very few radiologists buy them and the manufacturers are, therefore, not able to produce them in quantity and consequently have to sell the instruments at a relatively high price. Even then, they do not make any profit on them.

Listening to this wonderful group of papers given by the members of the Memorial Hospital staff, one is certainly encouraged to learn that such excellent results have

been obtained there through the co-operation of physicists and medical men. It makes one feel that after all the work of the physicist must have been of great importance in the working-out of dosage methods in the radiation therapy of cancer.

The Radiological Diagnosis of Hydatid Infection. C. C. Anderson. Brit. Jour. Radiol., November, 1928, I, n. s., p. 428.

Hydatid infection is one of the commonest parasitic diseases in New Zealand. The liver and lungs are the commonest sites of lodgment of the embryos and for the formation of cysts. When cysts are present in the liver, the chief radiological sign is an alteration of the normal diaphragmatic bow, which usually consists of a segmentation of the curve, although with large cysts one entire side of the diaphragm may be elevated. Except when death of the cyst contents has occurred, the complement-fixation test will be of much value for confirming a suspected diagnosis. When lime salts are deposited in the pericyst the diagnosis is usually readily made. With abdominal cysts located elsewhere than in the liver, a characteristic oval fluid collection may be demonstrated only by resorting to pneumoperitoneum.

In hydatid infection in the lungs, the X-ray appearances are fairly characteristic. A single cyst usually casts a homogeneous oval shadow and is apt to be located posteriorly near the base. The use of lipiodol is advocated for determining the size and location of these cysts which have communicated with a bronchus, been incompletely drained, and become infected. In obscure cases complicated by a pleurisy the diagnosis may remain in doubt until the pleurisy has resolved. The dangers attended with needling a hydatid cyst are emphasized.

J. E. Habbe, M.D.

TREATMENT OF EPITHELIOMA OF THE PENIS BASED ON A STUDY OF SIXTY CASES

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IN a paper on the Study of Eighteen Cases of Epithelioma of the Penis (1921) (1), an evaluation of the methods used at the State Institute was set forth. In the present paper I hope to supplement the value of the methods employed in the treatment of cancer of the penis by a report on 60 cases which have been treated at the Institute between the years 1914 and 1928. In this series there occurred 6 cases of malignant papilloma and 54 cases of epithelioma of the penis, as shown by histological examination.

The frequency of epithelioma of the penis has been given by various authors as from 1 to 3 per cent of all malignancy (2). In our statistics, based on 7,000 cases of malignant disease, only 60, or about eight-tenths of 1 per cent, were malignant disease of the penis.

The age incidence at the time of admission is depicted in Chart I. The oldest patient was 80 years, the youngest was 29.

TABLE I

Age incidence at the time of admission:

20-29	30-39	40-49	50-59	60-69	70-79	80-89
1 (1)	5 (2)	10	19 (2)	19 (1)	5	1

Note: The figure in parentheses indicates how many of these were malignant papillomas.

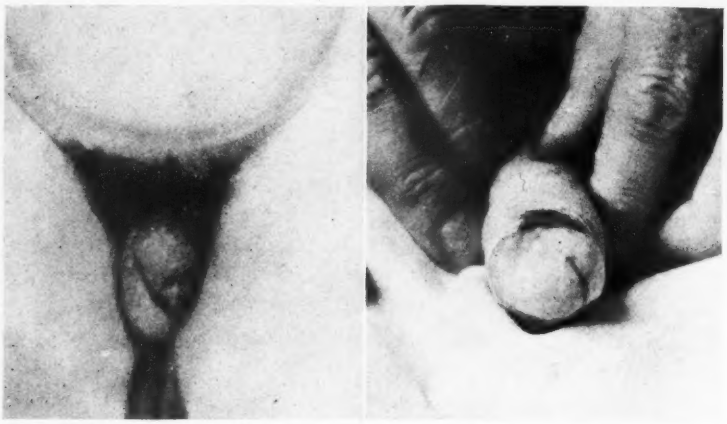
A history of cancer in the family was obtained in 12 cases. Fifty-two of these patients were married, 8 were unmarried. Syphilitic scars or venereal warts have been frequently recorded as etiological factors. In our cases there was a positive Wassermann reaction in 6 instances (one being a malignant papilloma); 16 gave a history of gonorrhea, and 5 of syphilis.

Phimosis has frequently been given as being a predisposing cause. Thomson describes a catarrhal balanitis occurring with phimosis which led to desquamation of epithelium and later to a hypertrophy of the epithelial cells, with overgrowth of the subepithelial connective tissue, to which Schuchardt gave the name *psoriasis preputialis*. It was previously supposed that the Jewish race and the Mohammedans, who practise circumcision early in life, were free from this disease, but Küttner (3) learned from the statistics of the Military Medical School at Constantinople that epithelioma of the penis did occur among the Mohammedans who had been circumcised. I have seen no cases of epithelioma of the penis in Jews. Among our 60 cases, 8 gave a history of circumcision prior to the beginning of the disease, 16 showed evidence of moderate or marked phimosis requiring dorsal slit in some instances to reveal the true nature of the disease. One case gave a history of circumcision followed within a year by epithelioma of the penis.

In four cases a history of injury was obtained which was definitely stated by the patient as being the beginning of his trouble. One man gave a history of injury to the penis by scalding six months before admission; one gave a history of an insect (Florida "red bug") bite eighteen months previous to the onset of the disease; one suffered laceration of the glans penis when struck by a pair of ice-tongs one year before the disease developed; another received an injury on the glans penis when struck by a plow handle a year and a half before he had a definite epithelioma.

References have been made to the possi-

bility of the transplantation of epithelioma by contact with malignant disease of the cervix. This is not borne out by our observation, as the frequency of epithelioma of the cervix in our statistics is about 15 per cent of all cancer, while the incidence of cancer of the penis is about 0.8 per cent. In two instances in this group of cases the patient's wife died of epithelioma of the cervix (one of these deaths occurred four years after the man had been apparently healed of his epithelioma of the penis).

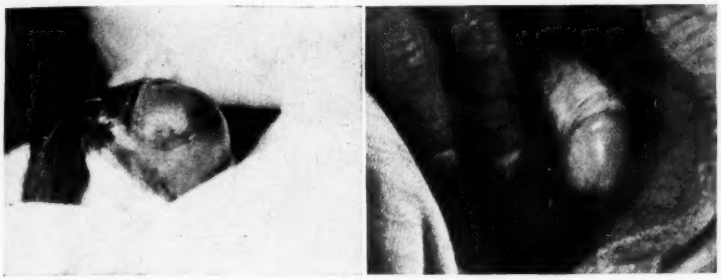


Figs. 1 and 2. Epithelioma of penis, before (*left*) and after (*right*) treatment.

In the diagnosis of epithelioma of the penis we must take into consideration the possibilities of syphilis and venereal warts. Early epithelioma of the penis may be regarded as a simple wart or an eroded papule, which is described as being more dense and pearly than a chancre, or as a smooth lump or thickening of the epithelium. During this stage there is little or no pain. As the disease progresses there is marked papillary or warty growth which soon begins to ulcerate, becomes cracked, infected, and suppurates. We have come to believe that all papillary growths on the glans penis are potentially malignant.

As a rule, local extension occurs relatively late but eventually there is invasion of the lymph channels. The superficial vessels drain into the inguinal nodes, or invasion may be along the deep lymphatics or the urethra, or along the vein of the penis into the pelvic nodes. The inguinal nodes are involved in the majority of cases when first seen, and in over 75 per cent of these cases it is bilateral. In some of the cases the inguinal nodes are markedly enlarged, due to infection rather than to metastases. This was proven by Küttner and bears out what we have observed in some of our cases. It is possible, as study has shown, that metastases may spread to the internal organs without involvement of the inguinal nodes. These metastases may occur in the liver or other internal organs. Rarely the disease is implanted by contact to the scrotum or to the skin of the thighs. Three autopsies were obtained in our cases of cancer of the penis, two of which showed widespread metastases, including the inguinal and retroperitoneal lymph nodes, the mediastinum, and in one case metastasis in the thyroid gland. It is of interest to note that the radical operation described in the textbook of genito-urinary diseases by Young and Davis does not include castration and the implantation of the urethra. In performing

radical operation on this type of malignant disease I have been in the habit of performing castration and transplanting the urethra, in view of having seen one case in which there was a distinct metastasis, showing pearl formation, in the testicle. This case also showed metastases in the lymph-bearing areas of both groins.



Figs. 3 and 4. Epithelioma of penis, before (*left*) and after (*right*) treatment.

The most common site for epithelioma of the penis is on the glans. In our 60 cases at the time of admission the lesion was definitely proven to have originated on the glans in 19 cases, in 27 the disease involved the glans and the prepuce, and in 11 the prepuce alone. These growths are either of the papillary type, especially on the glans penis, or are of the infiltrating epithelioma type, the usual one found on the prepuce. The histological structure of epithelioma of the penis shows numerous pearls and hornifications, which are also well marked in the metastases that occur in this disease. There were 6 cases of malignant papilloma. In these, there was marked surface proliferation, with little tendency to infiltration or metastasis; one case developed metastases in the groins and died in five years; another has metastases in both groins. Thick layers of irregular epithelial cells showing numerous mitotic figures arrange themselves upon a delicate framework of connective tissue. This type is comparatively benign.

The course of the disease is usually relatively slow before reaching the critical condition. Patients have been known to live eleven years without operation. The various authors give the mortality from cancer of the penis as about 32 per cent. Fifteen per cent of the cases develop visceral metastases. Recurrences are usually observed during the first year; a few occur in from one to five years, and an occasional case has been observed which recurred after eight years.

In 41 of our cases the history of the duration of the lesion was from six months to one year (5 of these were malignant papillomas); the remaining 19 gave a history of ulcerations or warty growths extending over periods of from two to fourteen years.

The treatment which these patients had had before consulting us varied from cautery of the wound and ointment applied, to X-ray treatment in two cases, radium in one, and partial or radical operation in two instances.

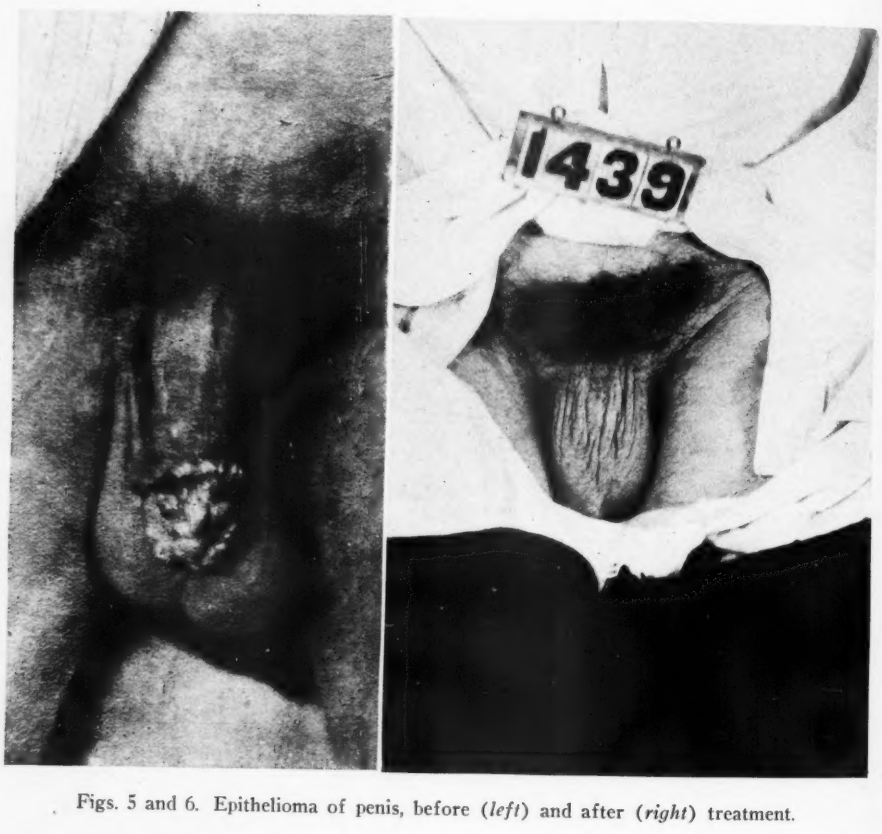
We have classified our cases in two groups:

Group I. The lesion confined to the penis.

Group II. A lesion on the penis, with definite metastases in the lymph-bearing areas of the groins.

These classifications were made clinically at the time of admission, including in Group

II all cases in which the lymph nodes were palpable and were thought to be metastatic. If subsequent operation proved that they were not metastatic, they were put in Group I. Dividing these case records in this way



Figs. 5 and 6. Epithelioma of penis, before (*left*) and after (*right*) treatment.

for study, 23 cases are classified as Group I and 37 as Group II.

TREATMENT USED IN THESE CASES

Where unfiltered X-rays were used the technic was 5 milliamperes, 140 kilovolts peak, no filter, time 6 to 8 minutes, depending on the thickness of the lesion, target skin distance 22 cm., making a total dosage of two to three times the erythema dose (5).

Treatment referred to as implantation with seeds.—Glass seeds were used up to 1927, averaging 1 mc. of radium emanation inserted for every cubic centimeter of the tumor. The factors of the high voltage X-ray given were: 200 kilovolts, 0.5 mm. Cu., dosage 130 per cent of the erythema dose, usually divided over a period of one week. (The period of time until the patient died or we lost trace of him has been figured from the date of our first examination.)

GROUP I (23 CASES)

Two cases treated with unfiltered X-rays on the penis resulted as follows: one has remained clinically well for ten years, the

other for eight one-half years (Figs. 1 and 2).

Four cases were treated with unfiltered X-rays applied to the primary lesion and high voltage or medium voltage X-rays to the groins, resulting as follows: in one case the lesion healed but recurred, with metastases, and the patient died in five years; two of these cases are clinically well after six and seven months, respectively; in another case the primary lesion healed and the patient died in two one-half years from another cause.

One case was treated with radium implantation into the primary lesion and high voltage X-rays over the groins, this patient now being clinically well three one-half years after (Figs. 3 and 4).

Five cases were treated with unfiltered X-rays or radium implantation of the primary lesion and with high voltage X-rays to the lymph-bearing areas, together with partial operation, resulting in their remaining well for seven years five months (Figs. 5 and 6), for seven years, for ten months, and in two instances for eight months, respectively. It is noteworthy that in one of these cases in which the partial operation was done nine months after radiation, because of scar and contracture, there was no evidence of malignancy in the tissue removed.

Two cases in which radiation of the lesion and the groins was followed immediately by radical operation, were clinically well three years and one year, respectively, afterward, but were then lost trace of.

Five other cases in which radical operation was performed from two to ten months after the radiation had been given, resulted as follows: one patient died from sepsis, one from hemorrhage (no evidence of malignancy in tissue removed), and the other three are now clinically well, after seven years, five years, and one year, respectively (Figs. 7 and 8).

Two cases had radical operation with no radiation: one lived six years without recurrence and died from cancer of the lip; the other died in two years from metastases to the region of the kidney.

Two other cases were radiated following radical operation, one remaining clinically well for eleven years, the other dying in six months from sepsis.

GROUP II (37 CASES)

One case was not treated and the patient died in two weeks' time.

One case, treated with unfiltered X-rays on the primary lesion, healed in two months, but the patient did not return for treatment of the groins and he died in one year ten months from metastases.

Thirteen cases were treated with unfiltered X-rays applied to the primary lesion and high voltage X-rays over the groins, resulting as follows: one was lost trace of, following treatment; another died in three months, without re-examination, of "apoplexy"; one patient who showed marked improvement of the local lesion for four months refused to return to continue treatment and died from the disease in one one-half years; one case showed improvement of the local lesion for one one-half years, refused operation, and died in two one-half years from the disease (he had colloidal lead treatment also); another who improved locally and refused operation died from the disease in five years; five showed temporary improvement of the lesion but died from the disease in one one-half years, one year three months, seven months, and six months (two cases), respectively; two were unimproved and died in three one-half months and two one-half months, respectively. In one case the primary lesion healed in five months, the patient had a recurrence one one-half years later, for which he was

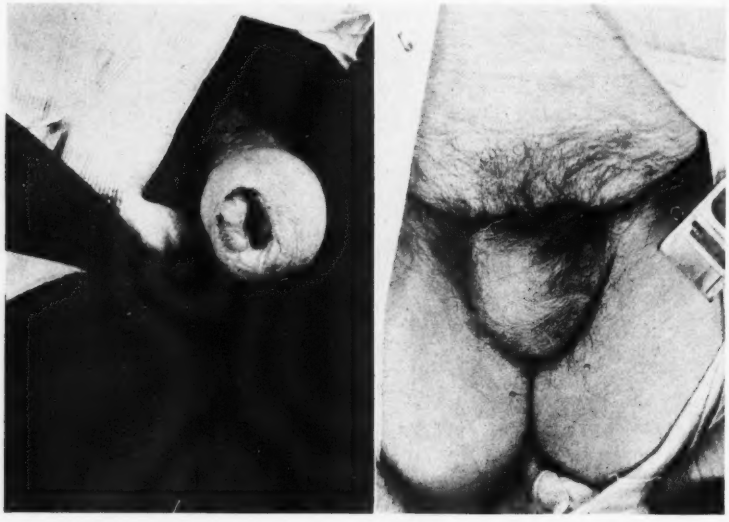
operated on, and he has now been well for five years.

One case had radium implantation of the local lesion, which healed in a few months, but the man did not return for further radiation over the groins and he died from the metastases one year ten months later.

One case had ulcers in the groins treated by radium applications, showed temporary improvement, but died in seven months from metastases.

Of seven cases having implantation of the primary lesion with radium, and high voltage X-rays over the groins, three improved locally in three months or more, and are now living—two one-half years, one year eight months, and four months, respectively. In one case the lesion has been healed for eight months, but at the present there is a question of recurrence in the groin (Figs. 9 and 10); one claimed to be well one year later, but has not been re-examined; the other two were unimproved and died in nine months and four months, respectively.

In one case partial operation was followed by high voltage X-rays over the groins; there was no local recurrence but the metastases began to increase in size in two one-half months and the man died in six months.



Figs. 7 and 8. Epithelioma of penis, before (*left*) and after (*right*) treatment.

In two cases the local lesion was implanted with radium and the nodes in the groins were treated with high voltage X-rays. In one of these the primary lesion healed in six months (over five years seven months previous to this report), a metastatic node was removed from the groin and radium implanted, and the man has been clinically well for over five years (Figs. 11 and 12). The other patient showed local improvement, amputation was performed three months after radiation, there was no local recurrence, but he died in one year one month from hemorrhage from the groin, due to ulceration of the metastasis.

Two cases had high voltage X-rays over the metastases in the groins ten years and one year, respectively, after amputation of the penis: the first has been clinically well for two years; in the second case the

metastases progressed and caused death in nine months.

There were three cases in which the primary lesion was treated with unfiltered X-rays and radical operation was performed in from four to nine months. One patient was clinically well for thirteen one-half years, and died of cardiovascular disease. Another died in nine months from the disease, and the third, who had low voltage X-rays over a mass which developed in the groin within a few months, died from the disease in one year four months.

Two cases having radical operation immediately, with high voltage X-rays over the groins, died—one in one year two months. In this instance there was no local recurrence but death was probably due to metastasis in the region of the kidney. The other patient had a recurrence in seven months and died in one year three months from hemorrhage from the groin, due to ulceration of the metastasis.

Figs. 9 and 10. Epithelioma of penis, before (*left*) and after (*right*) treatment.

Two cases had amputation of the penis and low or high voltage X-rays over the groins and radical operation two and three months, respectively, after radiation; they died, one in nine months from the disease and the other in one year from the metastasis which recurred in the groin.

One case had had radical operation three one-half months before admission and died

Figs. 11 and 12. Epithelioma of penis, before (*left*) and after (*right*) treatment.

in two months from the metastases, which were unaffected by radiation.

CONCLUSIONS

For Group I

1. Unfiltered X-ray alone has cured epithelioma of the penis in two instances, for ten years and for eight one-half years.

2. One case treated by implantation of the lesion with radium and high voltage X-rays over the groins is well, three one-half years later.

3. Unfiltered X-ray treatment of the local lesion, with high voltage X-ray over the groins, together with partial operation, has resulted in healings: two for seven years, one for ten months, and two for eight months.

4. Of the eleven cases in which radical operation and radiation were combined, six are living (for eleven years, seven years, five years, three years, one year, and one year, respectively); three died from operation; one died six years after from another cause; one died of internal metastasis in two years.

For Group II

1. Unfiltered X-ray or implantation of radium in the primary lesion, together with high voltage X-ray over the groins, has resulted in healing or great improvement in

the primary lesion, but as a rule the patients have died from their metastases.

2. The implantation of radium into the lesion, with removal of metastatic nodes and implantation of the groin, has resulted in healing in one case for five years.

3. Radical operation and thorough radiation was performed eight times, resulting in only one clinical cure (for thirteen one-half years); the other seven patients lived only from two months to one one-half years.

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Foreign Body in Nose, Diagnosed as Carcinoma, Unexpectedly Removed. M. C. Myerson. Laryngoscope, June, 1928, XXXVIII, 390.

The author reports a case of a girl, aged 16, who had been suffering with headaches for the past seven years, but recently had had an acute onset, with chill, temperature, general weakness, and swelling over the left malar region involving both lids of the left eye. An abscess formed in the region of the inner canthus of the left eye, which was drained. Three months later there was still some drainage and X-ray examination showed a shadow in the region of the left ethmoid which extended into the naris, also involving the left maxillary sinus. The findings suggested a newgrowth. An external operation of the Moure type for radical removal of a newgrowth was contemplated, but upon examination under anesthesia a foreign body was encountered which proved to be a mass of gauze 4½ inches long, impregnated with blood and tissue juices, and covered with granulation tissue. This was removed and the patient made an uneventful recovery.

B. C. CUSHWAY, M.D.

Investigations Regarding the Influence of Ultra-violet Rays on Avitaminosis. J. Krizenecky. Strahlentherapie, 1929, XXXI, 601.

Previous experiments have shown that pigeons living on a rice diet and guinea pigs living on an oats diet died from beriberi and scorbutus, respectively, in spite of exposure to a quartz mercury vapor lamp. The experiments were repeated, but this time the wave length 3,660 Ångstroms was singled out with a special filter and used in the treatment of the animals. The results were the same and the author concludes that even pure ultraviolet rays have no influence on the development of the avitaminosis.

E. A. POHLE, M.D., PH.D.

CASE REPORT

INTRA-UTERINE FRACTURE

CASE REPORT AND REVIEW OF ROENTGENOLOGIC FINDINGS

By HENRY SNURE, M.D., Los Angeles

It is the purpose of this paper to discuss chiefly the roentgenologic findings of intra-uterine fractures not associated with disease of the fetal osseous system, and to add one more case report. This type of fracture is rare; moreover, most of the reported cases antedate the general use of the roentgen ray, so that many of them are doubtful. There has apparently been only one attempt in the United States to collect and study true intra-uterine fractures, and that is the masterly review by Richard R. Smith (1). He carefully reviewed the literature on this subject, selected 43 cases that were most likely to be true intra-uterine fractures, although he stated some of them to be doubtful, and added one case of his own. His case was first examined by means of the roentgen ray eighteen days after birth and a reproduction of the roentgenogram included in the published report shows a fracture of the lower third of the tibial shaft, with angulation posteriorly, considerable callus along the anterior surface of the tibia, extending almost to the knee joint. The amount of callus present could be formed in eighteen days, as we know from a study of birth fractures. However, the leg and foot are smaller than normal, which suggests intra-uterine injury. The case history states that the deformity could not be changed manually at time of delivery, and that surgery was necessary to correct it later. Another reproduction of a roentgenogram is included, showing excellent position and callus formation, an examination which was presumably made some time after the last operation (two months after birth).

Fig. 1. Anteroposterior view of left femur made two hours after birth showing large amount of callus formation present.

In the collected cases the following had roentgen-ray examination: Case 43 (Heath) had a roentgen-ray examination at the age of four weeks, showing fracture of the tibia, apparently with non-union, together with areas of rarefied bone in distal ends of both tibia and fibula—this latter may have been due to disease. Circulation was good; no stigmata of congenital lues present; Wassermann not made.

Case 38 (Kirmisson), a boy eight years old, with angulation and pseudo-arthrosis of tibia. Roentgen-ray examination showed simply non-union at that time. Another film, made three months after osteotomy, showed union of the fibula, but not of the tibia. This boy also had congenital deformities of the toes.

In the early literature quite a number of cases are reported of bowing of the tibia, with malformation of the foot and toes, considered to be a clinical entity and ruled out of the fracture classification at that

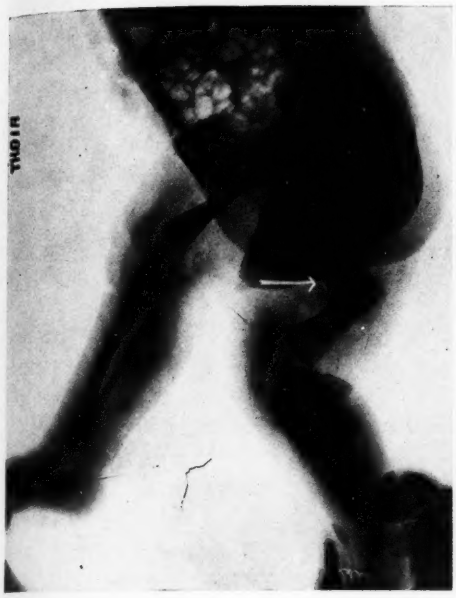

Fig. 2. Lateral view of left femur made two hours after birth. Note angulation and ossification centers.

Fig. 3. Lateral view seven weeks after birth. Heavy callus, with very little angulation.

time. Haudek (*2*), quoted by Smith, reported 97 cases of such deformities that were probably caused by amniotic bands. In none of the other cases reported was roentgen-ray examination mentioned; in fact, nearly all occurred before Röntgen's discovery of the X-ray.

Another case of intra-uterine fracture was reported recently by Dr. E. Filgueiras (*3*). This author publishes a roentgenogram of a clavicle fractured in midportion, with considerable callus formation present.

Statistics collected by Smith show 32 cases to have a single fracture, the most common being that of the clavicle (twelve cases). The skull and leg each have eleven, the forearm four, the humerus four, the femur three, the scapula one. To the above add one more fracture of the clavicle and my case of fracture of the femur.

From the roentgen-ray viewpoint, diseases of the fetus to be considered in intra-uterine fracture are three: Osteopsathyrosis, chondrodystrophies, and lues. These parade under a varied assortment of names.

Osteopsathyrosis, also known as *osteogenesis imperfecta.*—About 200 cases have been reported. These fractures usually are multiple; the bones have a normal outline on the film, but lack a sufficient amount of lime deposit—so much so that good roentgenograms with any degree of contrast are difficult to obtain. Very little callus is present until after birth. There is no bowing of the shafts or involvement of the epiphyses.

Chondrodystrophies.—In achondroplasia there is much shortening of the shafts, due to poor epiphyseal growth. The bone present is of normal texture and lime content. The shaft is widened at the epiphyseal line, with some irregularity of outline at this point. Dyschondroplasia occurs *in utero,* but is distinguished by multiple exostoses of the cortex, in addition to changes at the epiphyseal line.

Lues.—The bones have a normal amount

of lime, with typical punched-out areas of diaphysis at the epiphyseal line. There are usually multiple lesions and no deformities of the shaft. Periostitis quite frequently accompanies the above findings.

Fig. 4. Film made eighteen months after birth. Right femur remains slightly bowed. Left femur has completely re-established medullary canal, is straight in both anteroposterior and lateral views, and of same length as opposite femur. At nine months the changes were practically the same as at eighteen months.

CASE REPORT

Mrs. B. entered the hospital on the service of Dr. George E. Greenbaum, for Cæsarean section. The reasons given were: generally contracted pelvis; congenital hip dislocation, clinically present. A roentgenogram of the mother's pelvis shows what appear to be multiple cartilaginous exostoses, involving the epiphyseal lines of both femoral necks and causing marked deformity. As the patient was very fat, these deformities clinically resembled congenital hip dislocation. Exostoses present along rami of both pubic bones. Cæsarean section was done. The amount of amniotic fluid was less than usual; no amniotic bands were found; a small subserous fibroid was present. Marked deformity of the left femur was noted at time of delivery; otherwise the infant was normal.

Two hours after birth the baby was roentgenographed, with the following findings: A fracture of the left femur in the middle third of the shaft, with marked angulation posteriorly; callus formation abundant. From my experience with birth fractures, I believe it to have been of at least three weeks' duration. The whole body was roentgenographed, no other fractures or roentgen-ray evidence of disease being found. The normal number of ossification centers were present. The right femoral shaft showed considerable bowing or curvature, suggesting that the right femur was pressed down over the left for a period of time and that the left finally fractured.

Cause of the fracture was unknown, though it may have been due to trauma over the abdomen during intercourse, which was indulged in up to the last two weeks of pregnancy. The mother admits making two attempts at abortion during the first three months of pregnancy, which probably have no bearing on the fracture. In the orthopedic care, which was under the direction of Dr. Steele F. Stewart, the Truesdale fracture box was used. A small amount of weight was employed at first, as sufficient pull for perfect position caused cyanosis of the leg, apparently due to traction on a shortened femoral artery. The baby was roentgenographed frequently during the next eighteen months. She has been walking for about one month and no defects in gait are noted.

From the foregoing it can be stated that the roentgen ray definitely proves this case

to be a true intra-uterine fracture because (1) it shows the absence of disease; (2) it demonstrates normal repair of fractured bone, and (3) the roentgen-ray examination was made two hours after birth, thereby avoiding confusion with birth fractures, which may develop callus in eight days' time.

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THE AMERICAN COLLEGE OF SURGEONS

The American College of Surgeons will hold its nineteenth annual Clinical Congress in Chicago, October 14–18. Headquarters will be at the Stevens Hotel. An intensive program is being planned to make this home-coming event the greatest in the history of the College. The Hospital Standardization Conference will consist of morning and afternoon sessions on Monday to Thursday, inclusive. There will be a series of clinical demonstrations given by: George W. Crile, Cleveland; John B. Deaver, Philadelphia; John M. T. Finney, Baltimore; Charles H. Mayo, Rochester, and others. Monday evening's program will include an address of welcome by the Chairman of the Chicago Committee on Arrangements, Dr. Herman L. Kretschmer; the address of the retiring President, Dr. Franklin H. Martin, Chicago; the inaugural address of the new President, Major-General Merritte W. Ireland, Washington, D. C., and the John B. Murphy Oration in Surgery by Professor D. P. D. Wilkie, of Edinburgh. Among the foreign visitors will be: Dr. James Heyman, of Stockholm; Dr. Thierry de Martel, of Paris; Visconte Aguilar, of Madrid, and Mr. Herbert Tilley, of London. Tuesday, Wednesday, and Thursday evening sessions will consist of scientific papers presented by surgeons from the United States, Canada, and from abroad. The Annual Convocation of the College will be held on Friday evening. The Fellowship Address will be delivered by Dr. Glenn Frank, President of the University of Wisconsin. The annual meeting of the Governors and Fellows will be held Thursday afternoon, followed by symposia on cancer and bone sarcoma. An all-day session on Traumatic Surgery will be held on Friday, in which leaders in industry, labor, indemnity organizations, and the medical profession will participate. A special program has been arranged that will be of interest to those whose practice is limited to surgery of the eye, ear, nose, and throat. A feature of the Congress will be the showing of surgical films that have been produced under the supervision of and approved by the Board on Medical Motion Pictures of the College. New developments in color photography will be demonstrated. In addition to the commercial exhibits, there will be scientific exhibits by the departments of the College. A rate of one and one-half the regular one-way fare has been granted on railroads of the United States and Canada to those holding convention certificates.

EDITORIAL

M. J. Hubeny, M.D. . . . . *Editor*
Benjamin H. Orndoff, M.D.
John D. Camp, M.D. } *Associate Editors*

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THE UNIT OF THE ROENTGEN-RAY DOSE

Confusion seems to exist as to the manner of writing the dose unit for roentgen rays, the international "r-unit." A short statement of the question, therefore, seems to be necessary.

The unit of the roentgen-ray dose "one r" (designated by the small letter "r") was defined and adopted by the Second International Congress of Radiology, Stockholm, July 23–27, 1928. Roentgen doses should now be expressed only in this unit. The international "r-unit" replaces all similar dosage units which were used previously; these units were called the "e" or "E"-unit (electrostatic unit), the "R-unit" (electrostatic R-unit), and the French "R-unit." Although, for purposes of comparison, the "e," "E," and electrostatic "R-units" are practically identical in definition and value and also are identical with the "r-unit," the French "R" is defined differently and is approximately half of one international "r." Differences between the "American R-unit" and the "German R-unit," which once seemed to exist, also have been eliminated and both have been shown to be identical with the international "r-unit," provided a small temperature correction is made.

Detailed discussions on these various dosage units have appeared from time to time in this journal (see Radiology, 1926, VI, 320; 1927, VIII, 312; 1928, X, 284; 1929, XII, 317). Thus, when referring to the literature published previous to July, 1928, it may be necessary to employ one of the older terms for the dose unit: however, *since the adoption of the international "r-unit" only this unit should be used to express dosage* in papers to be published in the future.

Otto Glasser, Ph.D.
Cleveland Clinic.

PRELIMINARY PROGRAM

FIFTEENTH ANNUAL MEETING, DEC. 2 TO 6, INCLUSIVE, 1929, ROYAL YORK HOTEL, TORONTO

No attempt has been made at this time to set the day or hour for any special paper's presentation: those matters will be announced in the program to be prepared for mailing to the members immediately preceding the date of convening, and for use at the meeting. To avoid any possible confusion, the essayists' names in the following preliminary announcement appear in alphabetical sequence, grouped under papers, clinics, demonstrations, and symposia. The names of discussants will be announced later.

1. Paul Andrus, M.D., Queen Alexandria Sanatorium, London, Ontario, Canada
   "The Measurement and Control of Sharpness in Radiography."
2. John M. Barnes, M.D., Ann Arbor, Mich.
   "Radiographic Exposure in r-units."
3. D. S. Beilin, M.D., Chicago
   "When has Visceroptosis Clinical Significance?"

4. Webster W. Belden, M.D., New York City.
"Roentgenological Consideration of the Fifth Lumbar Vertebra."

5. E. S. Blaine, M.D., Chicago
(Title to be announced.)

6. Samuel Brown, M.D., Cincinnati
"Gastro-intestinal Obstructions."

7. John D. Camp, M.D., Rochester, Minn.
"Further Observations on the Roentgenological Manifestations of Gastrojejunal and Jejunal Ulcer."

8. L. J. Carter, M.D., Brandon, Man., Canada.
"A Report of 100 Consecutive Cases of Uterine Fibroid."

9. John R. Carty, M.D., New York City
"The Modification of the Biological Reaction of Living Tissue to X-radiation by Physical and Chemical Agents."

10. James T. Case, M.D., Chicago
"Roentgenological Aspects of Pancreatic Disorders."

11. William J. Cassidy, M.D., Detroit
"Head Injuries: X-ray Confirmation and the Subsequent Surgical Evaluation and Indications."

12. Arthur C. Christie, M.D., Washington, D. C.
Presentation of the Work of the Committee on the Cost of Medical Care.

13. E. E. Cleaver, M.D., Toronto
"Ulcerative Colitis."

14. Augustus W. Crane, M.D., Kalamazoo, Mich.
(Title to be announced.)

15. W. H. Dickson, M.D., Toronto
"The Influence of Diet on the Size and Shape of the Colon in Arthritics." (Radiological Aspect.)

16. Howard P. Doub, M.D., Detroit
"Roentgen Diagnosis and Treatment of Thymomata."

17. Edwin C. Ernst, M.D., St. Louis
(Title to be announced.)

18. G. Failla, D.Sc., New York City
"A New Instrument for Measuring X-radiation."

19. John T. Farrell, Jr., M.D., Philadelphia
"Roentgen Diagnosis of Lesions of the Esophagus."

20. Temple Fay, M.D., Philadelphia
(Title to be announced.)

21. Maurice Feldman, M.D., Baltimore
"Early Recognition of Gastric Ulcer and Carcinoma as Revealed by Roentgen-ray Studies."

22. A. A. Fletcher, M.D., Toronto
"The Influence of Diet on the Size and Shape of the Colon in Arthritics." (Clinical Aspect.)

23. R. K. Ghormley, M.D., Rochester, Minn.
"Pathological Studies of the Common Forms of Arthritis, and Their Relation to X-rays."

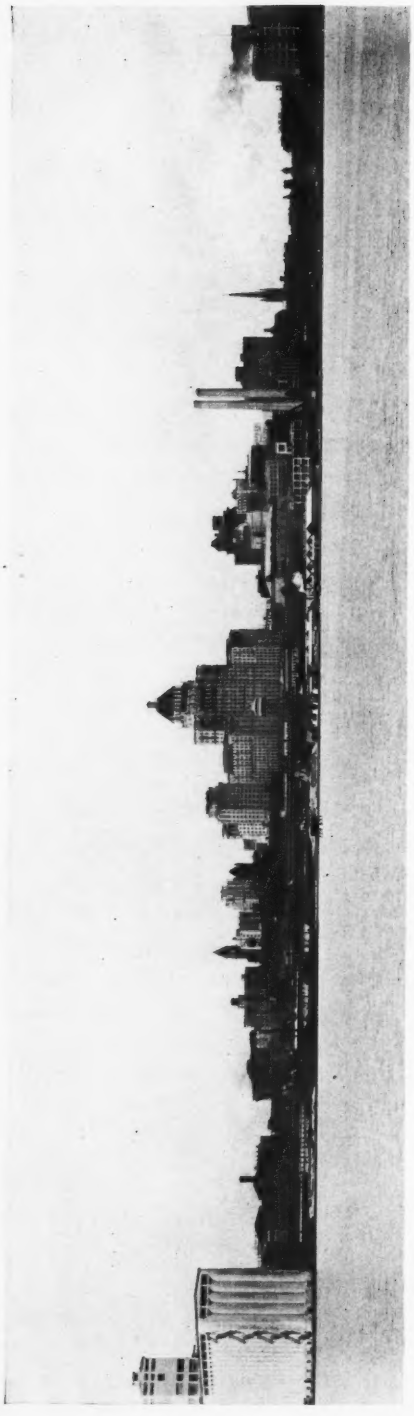
24. P. B. Goodwin, M.D., Peoria, Ill.
"Diagnosis of Urologic Diseases in Children by the X-ray."

25. Amedee Granger, M.D., New Orleans
"A Positive Sign of Extensive Destruction of the Mastoid in Infants."

26. George W. Grier, M.D., Pittsburgh
(Title to be announced.)

27. Preston M. Hickey, M.D., Ann Arbor, Mich.
"Lateral Teleoroentgenography of the Chest at Ten Feet."

28. I. Seth Hirsch, M.D., New York City
"Relation of the Pleuroperitoneal Cavity to Body Habitus."



The skyline of Toronto, in which the center is dominated by the Royal York Hotel and the tall buildings of the metropolitan district.

29. Fred Jenner Hodges, M.D., Madison, Wisc.
"Polypi of the Paranasal Sinuses."

30. Barbara Hunt, M.D., Bangor, Maine
"Report on the Use of Radium and Deep Therapy X-ray for the Last Seven Years in a Private Clinic in Maine, with Special Reference to the Problems of the Small Community."

31. Chevalier Jackson, M.D., Philadelphia
(Title to be announced.)

32. Hans A. Jarre, M.D., Detroit
"Roentgenologic Studies of Body Motion."

33. I. Warner Jenkins, M.D., Waco, Texas
"The Colon as a Primary Focus in the Causation of Disease."

34. E. L. Jenkinson, M.D., Chicago
(Title to be announced.)

35. Zoe Allison Johnston, M.D., Pittsburgh
"Some Skin Lesions Treated by Radium."

36. M. I. Kaplan, M.D., Chicago
(Title to be announced.)

37. Arnold H. Kegel, M.D., Chicago
"Fire Hazards."

38. B. R. Kirklin, M.D., Rochester, Minn.
(Title to be announced.)

39. James A. Larkin, M.D., Chicago
"Radium as a Cause of Death."

40. Leon T. LeWald, M.D., New York City
"Errors in Diagnosis of Pulmonary Tuberculosis."

41. Ira H. Lockwood, M.D., Kansas City, Mo.
"Bone Changes in the Spine in Hodgkin's Disease."

42. C. C. MACKLIN, M.D., University of Western Ontario, London, Ontario, Canada
"Researches on Bronchial Movements by the Aid of X-rays."

43. LAURENCE H. MAYERS, M.D., Chicago
(Title to be announced.)

44. H. B. MCEUEN, M.D., Jacksonville, Florida
"Reporting Six Cases of Melanoma, with Two of the Patients Well and Living over Five Years."

45. EDWIN A. MERRITT, M.D., Washington, D. C.
(Title to be announced.)

46. SHERWOOD MOORE, M.D., St. Louis
(Title to be announced.)

47. A. MUTSCHELLER, PH.D., New York City
(Title to be announced.)

48. B. H. NICHOLS, M.D., Cleveland
"Roentgenological Examination of the Ureters."

49. CARL S. OAKMAN, M.D., Muncie, Ind.
"Traumatic Luxation of the Coccyx."

50. HENRY K. PANCOAST, M.D., and TEMPLE FAY, M.D., Philadelphia
"Encephalography: Technic, Indications, and Contra-indications."

51. ROSWELL T. PETTIT, M.D., Ottawa, Ill.
"Histopathologic Examination by the Radiologist as a Guide to Radiation Therapy."

52. GEORGE E. PFAHLER, M.D., Philadelphia
"Study of the Base of the Skull, with Special Reference to Deep Perisinusitis: Technic."

53. HARRY B. PODLASKY, M.D., and G. W. STEVENS, M.D., Milwaukee
"Study of the Newborn Chest, with Special Reference to the Thymus Gland, Based on 750 Cases."

54. SIDNEY PORTIS, M.D., Chicago
"The Clinical Interpretation of Roentgen Findings in the Large Colon."

55. R. P. POTTER, M.D., Marshfield, Wisc.
(Title to be announced.)

56. EDITH H. QUIMBY, M.A., and GEORGE T. PACK, M.D., New York City
"Further Studies of the Skin Erythema with Combinations of Two Types of Radiation."

57. G. E. RICHARDS, M.D., and A. C. SINGLETON, M.D., Toronto
"The Radiological Demonstration of the Optic Foramina."

58. CASSIE B. ROSE, M.D., Chicago
"Lung Atelectasis."

59. J. NEWTON SISK, M.D., Madison, Wisc.
(Title to be announced.)

60. M. C. SOSMAN, M.D., Boston
"Osteoporosis and Xanthomatosis of the Cranial Bones."

61. IRVING F. STEIN, M.D., and ROBERT A. ARENS, M.D., Chicago
"Further Experience with Iodized Oil and Pneumoperitoneum in Gynecologic Diagnosis."

62. ROBERT S. STONE, M.D., San Francisco
"Echinococcus Involvement of Bone."

63. CHARLES G. SUTHERLAND, M.B. (Tor.), Rochester, Minn.
(Title to be announced.)

64. HAROLD SWANBERG, M.D., Quincy, Ill.
'The Pre-radium Treatment of Carcinoma of the Uterine Cervix."

65. LAURISTON S. TAYLOR, PH.D., Washington, D. C.
"Problems of International X-ray Standardization."

66. C. H. WARFIELD, M.D., Chicago
"Spontaneous Pneumoperitoneum."

67. W. W. WATKINS, M.D., Phoenix, Ariz.
"Fungous Infection, with Special Reference to the Respiratory Tract."

68. J. L. WEATHERWAX, M.A., and CHARLES ROBB, E.E., Philadelphia
"Determination of Radiation Values in Lung Tissue with Variable Qualities of Radiation."

69. HARRY M. WEBER, M.D., Rochester, Minn.
"Factors of Error in the Roentgenologic Diagnosis of Diseases of the Large Intestine."

70. R. T. WILSON, M.D., Temple, Texas
(Title to be announced.)

71. SANFORD WITHERS, M.D., Denver
(Title to be announced.)

Symposium: Cancer. ALBERT SOILAND, M.D., Los Angeles, *Chairman.*

72. GEORGE E. BINKLEY, M.D., New York City
"Carcinoma of the Rectum."

73. HARRY H. BOWING, M.D., Rochester, Minn.
"Results Obtained in the Treatment of Cancer of the Uterus with Radium and Roentgen Rays from 1915 to 1924, Inclusive."

74. BOWMAN C. CROWELL, M.D., Chicago
"Bone Sarcoma."

75. WILLIAM P. HEALY, M.D., New York City
"Carcinoma of the Cervix."

76. DOUGLAS QUICK, M.D., New York City
"Treatment of Growths of the Nasal Accessory Sinuses and Nasopharynx."

77. G. E. RICHARDS, M.D., Toronto
"The Treatment of Secondaries in Breast Carcinoma."

78. HENRY SCHMITZ, M.D., and C. W. H. HUEPER, M.D., Chicago
"The Malignancy Index in Carcinoma of the Uterine Cervix and Breast."

79. B. F. SCHREINER, M.D., Buffalo
(Title to be announced.)

80. ALBERT SOILAND, M.D., Los Angeles
"The Economic Aspect of the Cancer Problem."

81. B. P. WIDMANN, M.D., Philadelphia
"Radiation Technic for Cancer of the Mouth with Combinations of Gamma and Varying Qualities of High Voltage Roentgen Rays."

82. FRANCIS CARTER WOOD, M.D., New York City
(Title to be announced.)

Genito-urinary Symposium: U. V. PORTMANN, M.D., Cleveland, *Chairman.*

83. CHARLES HIGGINS, M.D., Cleveland
"Diagnosis of Tumors of the Upper Genito-urinary Tract."

84. W. E. LOWER, M.D., Cleveland
"Bladder Tumors."

85. B. H. NICHOLS, M.D., Cleveland
"Roentgen Interpretation of Tumors of the Genito-urinary Tract."

Skin Clinic and Symposium: ROLLIN H. STEVENS, M.D., Detroit, *Chairman.*

Dosimetry Demonstrations: ERNST A. POHLE, M.D., PH.D., Madison, Wisc. *Chairman.*

Heart Clinic: W. E. CHAMBERLAIN, M.D., San Francisco, *Chairman.*

Special Demonstration of Bone Lesions: JOSEPH C. BLOODGOOD, M.D., Baltimore, *Chairman.*

THE TORONTO MEETING

RAILROAD AND HOTEL INFORMATION

All those who are expecting to attend the meeting of the Radiological Society of North America at Toronto next December will be glad to learn that a rate of one and one-half fare for the round trip has been granted by the railroads from all points in the United States and Canada, providing 150 certificates are validated.

All who buy railroad tickets should demand a "Convention Certificate" with each ticket at the time of purchase, and immediately upon arrival at the meeting should deposit these "Certificates" with the railroad clerk at the Registration Desk at the meeting. As soon as 150 of these "Certificates" are deposited, they will be validated and depositors may then reclaim them at the desk. *These certificates will be good for one-half the regular fare returning over the same route,* and within reasonable limits. Announcements will be made from time to time at the meeting relative to this matter.

At all previous meetings it has been necessary to have 250 of these "Certificates" before the reduced fare would be granted, but at this meeting only 150 are necessary. A charge of twenty-five cents is made for the validation of each certificate.

These rates apply to all members, and members of their families, exhibitors and their families, and visitors and their families—in fact, all persons coming to Toronto for the meeting and their families; but failure to secure the "Convention Certificates" at the time of purchase of the tickets to Toronto, or failure to validate the same, will forfeit all rights to this rate. All "Certificates" must be deposited with my representative at the desk for certification that the holder is in attendance at the meeting, before the railroad agent will validate them.

As stated in a communication last month, under the head of "The Commercial Exhibit," the Royal York Hotel, in Toronto, is the largest hotel and the highest building in the British Empire. It is a magnificent building and a finely conducted hostelry.

In a conference in Chicago last winter, at which time the location and the date of this Toronto meeting were decided, the writer withheld his approval of the fixing of the meeting place until the representative of this hotel had made a very material reduction in the rates for all those attending this meeting, and it was only when this representative came down to what he declared to be the "rock-bottom" rates, that our objection was withdrawn. These rates are to be $4.50 per day for single rooms and $7.00 per day for double rooms—all with bath.

In order to secure these unusually low rates at this hotel, it will be necessary to make reservations ahead of time and to inform the hotel when arriving that you are in attendance upon the meeting of the Radiological Society. Therefore, all members, visitors, and exhibitors who expect to attend are urged to notify Dr. W. C. Kruger, Toronto Western Hospital, Toronto, Ontario, Canada (the Chairman of Hotels and Lodgings Committee), stating whether single or double room is desired, and stating also how many ladies will be in the party. *Do this immediately, while you have it in mind.*

Members, visitors, and exhibitors are urged to bring the ladies of their families with them to the Toronto meeting. At the 1928 Chicago meeting there were more ladies present than at any previous meeting, and all were glad that they came. At Toronto there will be opportunities to purchase certain articles of wearing apparel, such as furs, and such fabrics as silk, linen, etc., at much lower prices than anywhere in the United States. The cost of the entire trip may be saved upon these items alone. Each person may bring goods costing not in excess of $100 into the United States, duty

free. The Toronto Committees have plans for the entertainment of the ladies, and they are urged to come. All who attend will be well repaid in the pleasant friendships renewed and in new ones formed, in addition to the pleasures of the trip and the meeting.

All who expect to attend are again urged to notify the head of the Toronto Committee on Hotels, so that suitable and satisfactory arrangements may be made. This plan has upon former occasions resulted in all having adequate accommodations without unnecessary excess, and has proven to be the best method of handling the matter.

I. S. TROSTLER, M.D.

Manager of Commercial Exhibit and Transportation, The Radiological Society of North America.
812 Marshall Field Annex, Chicago.

RECOMMENDATIONS OF THE INTERNATIONAL X-RAY UNIT COMMITTEE[1]

THE SECOND INTERNATIONAL CONGRESS OF RADIOLOGY, STOCKHOLM, JULY 23-27, 1928

The following recommendations, put forward by the undersigned members of the International X-ray Unit Committee, were approved by the International Radiological Committee and adopted at a general meeting of the International Congress of Radiology, held at Stockholm, July 27, 1928.

1. That an International Unit of X-radiation be adopted.

2. That this International Unit be the quantity of X-radiation which, when the secondary electrons are fully utilized and the wall effect of the chamber is avoided, produces in one cubic centimeter of atmospheric air at 0° C. and 76 cms. mercury pressure, such a degree of conductivity that one electrostatic unit of charge is measured at saturation current.

3. That the International Unit of X-radiation be called the "roentgen" and that it be designated by the letter small "r."

4. That various standard methods be employed to establish the unit.

5. That for all comparative purposes it is advisable to employ ionization chambers which have been calibrated in terms of a standard chamber for X-radiation of the various qualities employed. It is also advisable to make the wall effects of these chambers as small as possible.

6. That the practical instrument used to measure X-ray output be called a dosage meter (Dosismesser, dosimètre).

7. That the constancy of the indications of the dosage meter be tested by means of gamma radiation emitted from a definite quantity of radium element, the measurement being carried out always under the same conditions.

8. That any specifiation of dosage is incomplete without specifying the quality as well as the quantity of the radiation. The quality of X-radiation used for practical purposes is very varied and it would be impracticable to give a complete specification of it; but much information can be obtained from a knowledge of the degree of absorption of the radiation in standard materials, the peak voltage applied to the tube, together with the filter employed, and the general character of the high tension apparatus.

For practical purposes the quality may be expressed by stating the half value layer in a suitable material, or by stating the effective wave length as determined by the percentage amount of radiation transmitted through a given thickness of a suitable material (copper or aluminium).

In view of the fact that rapid progress is being made in methods of X-ray measurement and in our knowledge of X-ray phe-

[1]Received for publication August 24, 1929.

nomena the Committee feels that the above recommendations should be regarded as being of a provisional character.

M. SIEGBAHN, *Chairman*, Sweden
E. A. OWEN, Great Britain, and H. HOLTHUSEN, Germany, *Hon. Secretaries*
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N. S. FINZI, Great Britain
J. GRAU CASAS, Spain
E. C. ERNST, United States
H. BEHNKEN, Germany

SCIENCE IN "THE CENTURY OF PROGRESS"

The achievements made in the medical and allied professions during the past one hundred years through the aid of pure and applied science may be graphically shown at the Chicago World's Fair Centennial Celebration to be held in 1933. Leading authorities in these professions have been invited to serve on the National Research Council Science Advisory Committee to the Fair. They have been asked to advise ways and means as to how to interpret in a tangible form the advances made since applied science entered their respective fields.

The medical men serving on the general committee include such well known men as Prof. R. R. Bensley, of the Department of Anatomy, University of Chicago, on anatomy; Dean Arthur D. Black, of the dental school of Northwestern University, dentistry; Dr. Frank Billings, of Chicago, medicine; Prof. Preston M. Hickey, of the Medical School of the University of Michigan, on roentgenology; Prof. Stanhope Bayne-Jones, of the School of Medicine and Dentistry of Rochester University, bacteriology; Prof. Fay-Cooper Cole, Department of Anthropology, University of Chicago, anthropology, and Prof. Harvey A. Carr, Department of Psychology, University of Chicago, psychology.

The National Research Council Science Advisory Committee was formed at the request of the trustees of the Chicago Exposition. As the most far-reaching scientific body in the United States, the trustees asked the National Research Council to prepare for a world's fair of an entirely different character than any exposition ever held before. This exposition of the advancement of science is to deal with the progress made by pure and applied science in industry since the beginning of the so-called Industrial Revolution, up to the present time. It is planned to make science one of the dominant notes of the Exposition.

Leading engineers and scientists from all sections of the United States are members of this general advisory committee and they will strive to formulate a plan for the exposition that may be suggested as a basic scheme for the Fair. The members of the general committee will submit to the executive committee ideas which it is hoped to coordinate into a central working plan by early Fall, 1929.

As now planned, the Chicago World's Fair Centennial Celebration, which will be known as "The Century of Progress," will probably offer the most unusual opportunity

in the history of science for a physical demonstration of the progress of pure and applied science in the development of industry.

The Science Advisory Committee is headed by an executive committee, the members of which are: Dr. Frank B. Jewett, New York, *Chairman;* Dr. George K. Burgess, Washington, D. C.; Dr. Vernon Kellogg, Washington, D. C.; Gano Dunn, New York; Prof. M. I. Pupin, New York, and Dr. William Allen Pusey, of Chicago.

Maurice Holland, of New York, has been appointed Executive Secretary of the Committee, which has established offices at 40 West 40th Street, New York City.

ILLNESS OF WALTER T. BRONSON, M.D., SECRETARY AND TREASURER OF THE SOCIETY

Dr. Bronson's many friends in the Society will be concerned to learn of his illness, but cheered by the news of a satisfactory convalescence. Meanwhile, Dr. I. S. Trostler, 25 East Washington St., Chicago, is serving as Acting Secretary-Treasurer.

CLINICAL CONGRESS AND EIGHTH ANNUAL MEETING OF THE AMERICAN COLLEGE OF PHYSICAL THERAPY

NOVEMBER 4, 5, 6, AND 7, 1929
HOTEL SHERMAN, CHICAGO

Chicago has again been selected as the annual meeting place for the clinical congress of physical therapy of the American College of Physical Therapy. The consensus of opinion of the many representatives who have attended the sessions in the past few years is that Chicago offers the most attractive features for a large medical gathering. Convention facilities are unsurpassed. Chicago as a medical center needs no apology. The experience of those who have attended any of the previous conventions speaks well for a highly successful 1929 Clinical Congress.

One of the novel features to be inaugurated this year is the clinical part of the program. One-half of each day will be devoted to a variety of clinics in the sections on Medicine, Surgery and allied specialties, and Eye, Ear, Nose, and Throat. As in the past, there will also be a joint meeting of all sections for the presentation of numerous addresses of interest to all physicians, irrespective of their specialties. Education in physical therapy will be thoroughly stressed, as the time has come when this phase of the subject must be given due emphasis by an organization such as the American College of Physical Therapy. Scientific papers, clinical addresses, demonstrations of technic, and scientific and technical exhibits will comprise the remainder of a scientific program which merits the attention of all those interested in the newer fields of medicine. Attendance at the Congress is not limited to the Fellows of the College, as all duly licensed physicians, their technicians and assistants, properly sponsored, are cordially invited to attend all the sessions.

Program and other information may be obtained by writing to the Executive Offices, American College of Physical Therapy, Suite 716, 30 N. Michigan Avenue, Chicago, Illinois.

ABSTRACTS OF CURRENT LITERATURE

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Ultra-violet Therapy in Otorhinolaryngology. A. J. Cemach. Strahlentherapie, 1929, XXXII, 361.

This is a well illustrated article relating the technic and indications for light therapy in diseases of the ear, nose, and throat. It does not lend itself well to abridgment and should be looked up in the original text by everyone interested in this type of treatment.

E. A. POHLE, M.D., PH.D.

An Analysis of Vertebral Anomalies. Theodore A. Willis. Am. Jour. Surg., February, 1929, VI, 163.

This report is the result of a study of fourteen hundred skeletons. From an etiological standpoint, the author classified these anomalies into three groups, the effects of three distinct factors: phylogenetic, developmental, and acquired. The anomalies which he terms phylogenetic, because they represent stages in evolutionary shortening of the spinal column, include sacralization of the twenty-fourth vertebral segment, asacralization of the twenty-fifth, large transverse processes of the last lumbar, and variations in the articular processes of the lumbosacral articulation. Among these developmental anomalies the most commonly recognized is the bifid neural arch. Variations in the articular processes, particularly of the lumbosacral articulation, are sometimes found. Deformities of the neural arch are rather frequently found. The separation of the neural arch occurs in the lamina between the superior and inferior articular processes. This is a most important factor in spondylolisthesis. Willis believes that when there is actual separation of the neural arch, it is the result of trauma, but that there is a pre-existing defect present.

Under "acquired defects" are included those due to injury and disease, the most frequent lesions being due to fractures and arthritis.

In the author's opinion, it is questionable if sacralization plays a very large part in symptoms referable to the lower back. It is also questionable if enlarged transverse processes of the lumbar vertebræ are frequently responsible for symptoms in this area. He believes that lack of spinous processes and laminæ weaken the back and predispose to strain, which, if neglected, may become chronic. He has found an unusually large percentage of cases of fusion of the sacro-iliac joints in this series.

H. P. DOUB, M.D.

X-ray Therapy of Brain Tumors in Childhood. Paul P. Gotthardt. Strahlentherapie, 1929, XXXI, 720.

During five years, there were 19 cases of brain tumor in children treated by roentgen rays. The irradiation used was 180 K.V., 0.5 Cu., or, in very superficial tumors, 160 K.V. through 3.0 Al. Four or five fields were given 15 to 20 per cent H.E.D. each in one sitting. Every two days one field was irradiated, giving a total dose of from 60 to 80 per cent on each single field. These series should not be repeated before intervals of six weeks.

Three children were immediately and permanently improved; the oldest case was under observation for 49 months. In seven cases there was a temporary improvement, while in six other cases, no influence whatsoever could be seen. One case did not return; in two other cases, the treatment could not be carried out completely — one of these two children died, while the other is still alive after five years.

It is suggested to irradiate all inoperable brain tumors in children, even if only temporary relief can be gained. No disturbance of the growth of the brain due to irradiation has been observed.

E. A. POHLE, M.D., PH.D.

Treatment of Mouth and Face Conditions by Irradiation. Ira I. Kaplan. Am. Jour. Roentgenol. and Rad. Ther., May, 1928, XIX, 437.

For malignant lesions about the face and neck deep X-ray therapy and radium emanation are combined. In all cases small heavily filtered doses given over a long period of time is the method of treatment, rather than intensive doses at frequent intervals. In many mouth lesions dental hygiene and mouth disinfection should be carried out before radiation is instituted. Biopsy is done in all cases. Roentgen rays are first applied over the lymphatic drainage areas, and radium therapy to the primary tumor follows immediately. By this plan of treatment severe reactions are avoided and necrosis occurs but rarely.

J. E. HABBE, M.D.

Radiation Therapy in the Treatment of Some Common Benign and Malignant Tumors, with Particular Reference to the Results Obtained at the Radium Center in Copenhagen. Edv. Collin. Acta Radiologica, 1929, X, Fasc. 2, p. 186.

The author, who is Chief of the Roentgen Clinic of the Finsen Institute, introduces his paper with some pertinent remarks on statistics, in which he points out that large series are based on material treated by a technic so varied that it is hardly possible to form a true and entirely satisfactory estimate of the therapy which has brought about the reported end-results. This fact, added to the long observation time essential and the diverse opinions relative to selecting cases for treatment, results in the statistics from various hospitals and clinics being confusing rather than informing. In the present paper are reported five years' unselected cases (that is, no case was turned away on the ground of being too bad) treated by a technic more or less uniform.

Four tabulations epitomize the cases, added to which are case reports and observations covering groups of tumors. The technic employed is based, in the main, on methods indicated by Dr. Gösta Forssell, and is given in detail for each type of lesion.

M. INGLEHART.

Carcinoma and Ulcer of the Stomach. E. M. Eberts. Can. Med. Assn. Jour., August, 1928, XIX, 145.

The author sums up the various clinical and laboratory methods used to make an early differentiation between gastric ulcer and gastric carcinoma, and concludes that there is as yet no reliable clinical sign or test for early carcinoma of the stomach.

In all cases of chronic gastric disorders, appearing after the age of forty, irrespective of whether the lesion is thought to be ulcer or cancer, the abdomen should be opened and the stomach directly examined. Even then the experienced surgeon often finds it impossible to say whether the lesion is benign or malignant. The percentage of error may be as high as 20 per cent. The conclusion is reached that all gastric lesions, whether diagnosed as ulcer or cancer, must be subjected to immediate radical excision.

L. J. CARTER, M.D.